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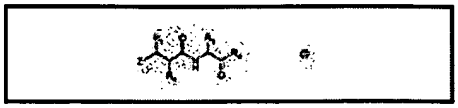

**(57) Abstract**
Compounds of formula (I) are antibacterial agents wherein: Z represents a radical of formula -N(OH)CH(=O) of formula -C (=O)NH(OH) and $R_1$-$R_4$ are as defined in the specification.

Description Claims

Antimicrobial Agents This invention relates to a novel class of hydroxamic acid and N-formyl hydroxylamine derivatives having antibacterial activity, and to pharmaceutical and veterinary compositions comprising such compounds.

Background to the Invention In general, bacterial pathogens are classified as either Gram-positive or Gram- negative. Many antibacterial agents (including antibiotics) are specific against one or other Gram-class of pathogens. Antibacterial agents effective against both Gram- positive and Gram-negative pathogens are therefore generally regarded as having broad spectrum activity.

Many classes of antibacterial agents are known, including the penicillins and cephalosporins, tetracyclines, sulfonamides, monobactams, fluoroquinolones and quinolones, aminoglycosides, glycopeptides, macrolides, polymyxins, lincosamides, trimethoprim and chloramphenicol. The fundamental mechanisms of action of these antibacterial classes vary.

Bacterial resistance to many known antibacterials is a growing problem. Accordingly there is a continuing need in the art for alternative antibacterial agents, especially those which have mechanisms of action fundamentally different from the known classes.

Amongst the Gram-positive pathogens, such as Staphylococci, Streptococci, Mycobacteria and Enterococci, resistant strains have evolved/arisen which makes them particularly difficult to eradicate. Examples of such strains are methicillin resistant Staphylococcus aureus (MRSA), methicillin resistant coagulase negative Staphylococci (MRCNS), penicillin resistant Streptococcus pneumonie and multiply resistant Enterococcus faecium.

Pathogenic bacteria are often resistant to the aminoglycoside,-lactam (penicillins and cephalosporins), and chloramphenicol types of antibiotic. This resistance involves the enzymatic inactivation of the antibiotic by hydrolysis or by formation of inactive derivatives. The ß-lactam (penicillin and cephalosporin) family of antibiotics are characterised by the presence of a ß-iactam ring structure. Resistance to this family of antibiotics in clinical isolates is most commonly due to the production of a "penicillinase" ( (3-lactamase) enzyme by the resistant bacterium which hydrolyses the p-tactam ring thus eliminating its antibacterial activity.

Recently there has been an emergence of vancomycin-resistant strains of enterococci (Woodford N. 1998 Glycopeptide-resistant enterococci: a decade of experience. Journal of Medical Microbiology. 47 (10): 849-62). Vancomycin-resistant enterococci are particularly hazardous in that they are frequent causes of hospital based infections and are inherently resistant to most antibiotics. Vancomycin works by binding to the terminal D-Ala-D-Ala residues of the cell wall peptidioglycan precursor. The high-level resistance to vancomycin is known as VanA and is conferred by a genes located on a transposable

element which alter the terminal residues to D-Ala-D-lac thus reducing the affinity for vancomycin.

In view of the rapid emergence of multidrug-resistant bacteria, the development of antibacterial agents with novel modes of action that are effective against the growing number of resistant bacteria, particularly the vancomycin resistant enterococci and P-lactam antibiotic-resistant bacteria, such as methicillin-resistant Staphylococcus aureus, is of utmost importance.

Brief Description of the invention This invention is based on the finding that certain hydroxamic acid and N-formyl hydroxylamine derivatives have antibacterial activity, and makes available a new class of antibacterial agents. The inventors have found that the compounds with which this invention is concerned are antibacterial with respect to a range of Gram- positive and Gram-negative organisms.

Although it may be of interest to establish the mechanism of action of the compounds with which the invention is concerned, it is their ability to inhibit bacterial growth that makes them useful. However, it is presently believed that their antibacterial activity is due, at least in part, to intracellular inhibition of bacterial polypeptide deformylase (PDF; EC 3.5.1.31).

All ribosome-mediated synthesis of proteins starts with a methionine residue. In prokaryotes the methionyl moiety carried by the initiator tRNA is N-formylated prior to its incorporation into a polypeptide. Consequently, N-formylmethionine is always . present at the N-terminus of a nascent bacterial polypeptide. However, most mature proteins do not retain the N-formyl group or the terminal methionine residue.

Deformylation is required prior to methionine removal, since methionine aminopeptidase does not recognise peptides with an N-terminal formylmethionine residue (Solbiati et al., J. Mol. Biol. 290: 607-614,1999). Deformylation is, therefore, a crucial step in bacterial protein biosynthesis and the enzyme responsible, PDF, is essential for normal bacterial growth. Although the gene encoding PDF (def) is present in all pathogenic bacteria for which sequences are known (Meinnel et al., J.

Mol. Biol, 266: 939-49,1997), it has no eukaryotic counterpart, making it an attractive target for antibacterial chemotherapy.

The isolation and characterisation of PDF has been facilitated by an understanding of the importance of the metal ion in the active site (Groche et al., Biophys. Biochem.

Res. Commun., 246: 324-6,1998). The Fe2+ form is highly active in vivo but is unstable when isolated due to oxidative degradation (Rajagopalan et al., J. Biol.

Chem. 273: 22305-10,1998). The Ni2+ form of the enzyme has specific activity comparable with the ferrous enzyme but is oxygen-insensitive (Ragusa et al., J. Mol.

Biol. 1998,280: 515-23,1998). The Zn2+ enzyme is also stable but is almost devoid of catalytic activity (Rajagopalan et al., J. Am. Chem. Soc. 119: 12418-12419,1997).

Several X-ray crystal structures and NMR structures of E. coli PDF, with or without bound inhibitors, have been published (Chan et al., Biochemistry 36: 13904-9,1997 ; Becker et al., Nature Struct. Biol. 5 : 1053-8,1998; Becker et al., J. Biol. Chem.

273: 11413-6,1998; Hao et al., Biochemistry, 38: 4712-9,1999; Dardel et al., J. Mol.

Biol. 280: 501-13,1998; O'Connell et al., J. Biomol. NMR, 13: 311-24,1999), indicating similarities in active site geometry to metalloproteinases such as thermolysin and the metzincins.

Recently the substrate specificity of PDF has been extensively studied (Ragusa et al., J. Mol. Biol. 289: 1445-57,1999; Hu et al., Biochemistry 38: 643-50,1999; Meinnel et al., Biochemistry, 38: 4287-95,1999). These authors conclue that an . unbranched hydrophobic chain is preferred at P1', while a wide variety of P2' substituents are acceptable and an aromatic substituent may be advantageous at the P3'position. There have also been reports that small peptidic compounds containing an H-phosphonate (Hu et al., Bioorg. Med. Chem. Lett., 8: 2479-82,1998) or thiol (Meinnel et al., Biochemistry, 38: 4287-95,1999) metal binding group are micromolar inhibitors of PDF. Peptide aldehydes such as calpeptin (N-Cbz-Leu- norleucinal) have also been shown to inhibit PDF (Durand et al., Arch. Biochem.

Biophys., 367: 297-302,1999). However, the identity of the metal binding group and its spacing from the rest of the molecule ("recognition fragment") has not been studied extensively. Furthermore, non-peptidic PDF inhibitors, which may be desirable from the point of view of bacterial cell wall permeability or oral bioavailability in the host species, have not been identified.

Recently it has been reported that PDF is present in eukaryotic parasites such as Plasmodium falciparum (Ferreira et al, Parasitology Today, vol 16, no. 4,2000).

Those authors also found evidence for the presence of PDF in other parasites of humans, such as the kinetoplastid protozoan parasites Trypanosoma brucei and Leishmania major. Based on these findings, it is anticipated that the compounds with which this invention is concerned have antiprotozoal activity, and are useful in the treatment of malaria and other protozoal diseases.

Certain N-formyl hydroxylamine derivatives have previously been claimed in the patent publications listed below, although very few examples of such compounds have been specifically made and described: EP-B-0236872 (Roche) WO 92/09563 (Glycomed) WO 92/04735 (Syntex) WO 95/19965 (Glycomed) WO 95/22966 (Sanofi Winthrop) WO 95/33709 (Roche) WO 96/23791 (Syntex) WO 96/16027 (Syntex/Agouron) WO 97/03783 (British Biotech) WO 97/18207 (DuPont Merck) WO 98/38179 (GlaxoWellcome) WO 98/47863 (Labs Jaques Logeais) The pharmaceutical utility ascribed to the N-formyl hydroxylamine derivatives in those publications is the ability to inhibit matrix metalloproteinases (MMPs) and in some cases release of tumour necrosis factor (TNF), and hence the treatment of diseases or conditions mediated by those enzymes, such as cancer and rheumatoid arthritis. That prior art does not disclose or imply that N-formyl hydroxylamine derivatives have antibacterial activity.

In addition to these, US-A-4,738,803 (Roques et al.) also discloses N-formyl hydroxylamine derivatives, however, these compounds are disclosed as enkephalinase inhibitors and are proposed for use as antidepressants and hypotensive agents. Also, WO 97/38705 (Bristol-Myers Squibb) discloses certain N- formyl hydroxylamine derivatives as enkephalinase and angiotensin converting enzyme inhibitors. This prior art does not disclose or imply that N-formyl hydroxylamine derivatives have antibacterial activity either.

Our copending International patent applications nos. WO 99/39704 and WO 99/59568 disclose that certain N-formyl hydroxylamine and hydroxamic acid derivatives have antibacterial activity. One class of compounds disclosed therein as having such activity has general formula (IA): Wherein X represents an N-formylhydroxylamino group (-N (OH) CHO) or a hydroxamic acid group (-CONHOH), and the various"R"substituents are as specified in the documents. The compounds useful in accordance with the present invention differ in structure from those of WO 99/39704 and WO 99/59568 principal in that the

amido radical R6R5NCO-is replaced by a ketone radical.

Very many hydroxamic acid derivatives are known. Many have been disclosed as having matrix metalloproteinase (MMP) inhibitory activity, and thus to be potentially useful for the treatment of diseases mediated by MMPs, for example cancer, arthritides, and contitions involving tissue remodeling such as wound healing, and restenosis. However, very few such known hydroxamic acid derivatives have the ketone moiety which characterises the compounds useful according to the present invention. One publication which does, however, is WO 98/30541 (Abbott).

Detailed description of the invention According to the first aspect of the present invention there is provided the use of a compound of formula (I) or a pharmaceutically or veterinarily acceptable salt, hydrate or solvate thereof in the preparation of a composition for treatment of bacterial or protozoal infections in humans and non-human mammais: wherein: Z represents a radical of formula-N (OH) CH (=O) or formula-C (=O) NH (OH); Ri represents hydrogen, methyl or trifluoromethyl, or, except when Z is a radical of formula-N (OH) CH (=O), a hydroxy or amino group; R2 represents a group R10-(X)n-(ALK)m-wherein R, o represents hydrogen, or a C,-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, cycloalkyl, aryl, or heterocyclyl group, any of which may be unsubstituted or substituted by (C,-C6) alkyl, (C,-C6) alkoxy, hydroxy, mercapto, (C,-C6) alkylthio, amino, halo (including fluoro, chloro, bromo and iodo), trifluoromethyl, cyano, nitro, oxo,-COOH,-CONH2.-COORA,-NHCORA,-CONHRA,-NHRA,-NRARB, or-CONR wherein RA and R8 are independently a (C,-C6) alkyl group and ALK represents a straight or branched divalent C,-C6 alkylene, C2-C6 alkenylene, or C2-C6 alkynylene radical, and may be interrupted by one or more non-adjacent-NH-,-O-or-S-linkages, X -O-or-S-,and-NH-, m and n are independently 0 or 1; R3 represents the side chain of a natural or non-natural alpha amino acid; and R4 represents a radical R5- (ALK) P- wherein ALK is as defined in relation to R2, p is 0 or 1, and R5 represents hydrogen, or a C,-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, cycloalkyl, aryl, or heterocyclyl group any of which (i) may be substituted by a group selected from (C,-C6) alkyl, phenyl, benzyl, (Ci-Ce) alkoxy, phenoxy, hydroxy, mercapto, (C,-C6) alkylthio, amino, halo, trifluoromethyl, cyano, nitro, oxo,-COOH,-SO2H,-CONH2-SO2NH2,-CORA, -SO2RA,-COORA,-CONHRA,-SO2NHRA,-NHCORA,-SORA,-SO2RA, -NHSO2RA, and-NHRA, wherein RA is (C,-C6) alkyl, cycloalkyl, phenyl, 2-, 3-or 4-pyridyl, N-or 2-, 3-or 4- piperidyl, N-or 2-or 3-piperazyl group; or (ii) may be substituted by-NRAR3,-CONRARB or-SO2NRARB, wherein RA and R3 are independently (Ci-Ce) alkyl, cycloalkyl, phenyl, 2-, 3-or 4-pyridyl, N-or 2-, 3-or 4- piperidyl, N-or 2-or 3-piperazyl group, or when taken together with the N atom to which they are attached RA and RB form a 5 to 7 membered aromatic or non-aromatic ring, which ring (a) may contain addition heteroatoms selected from N, O and S, and in which any S atom may be oxidised as a sulphonyl or sulphoxide, and (b) may be substituted on a ring carbon or heteroatom by one or more of the substituents listed under (i) above.

In another aspect, the invention provides a method for the treatment of bacterial or protozoal infections in humans and non-human mammals, which comprises administering to a subject suffering such infection an antibacterially effective dose of a compound of formula (I) as defined above.

In a further aspect of the invention there is provided a method for the treatment of bacterial contamination by applying an antibacterially effective amount of a compound of formula (I) as defined above to the site of contamination.

The compounds of formula (I) as defined above may be used as component (s) of antibacterial cleaning or disinfecting materials.

Compounds of formula (I) above wherein Z is a radical of formula-N (OH) CH (=O), are believed to be novel. Accordingly, in another aspect, the invention provides a compound of formula (I) wherein Z is a radical of formula-N (OH) CH (=O), or a pharmaceutically or veterinarily acceptable salt, hydrate or

solvate thereof.

On the hypothesis that the compounds (I) act by inhibition of intracellular PDF, the most potent antibacterial effect may be achieved by using compounds which efficiently pass through the bacterial cell wall. Thus, compounds which are highly active as inhibitors of PDF in vitro and which penetrate bacterial cells are preferred for use in accordance with the invention. It is to be expected that the antibacterial potency of compounds which are potent inhibitors of the PDF enzyme in vitro, but are poorly cell penetrant, may be improved by their use in the form of a prodrug, ie a structural modified analogue which is converted to the parent molecule of formula (I), for example by enzymic action, after it has passed through the bacterial cell wall.

The same is true in the case of protozoa.

As used herein the term" (C1-CÕ) alkyl"means a straight or branched chain alkyl moiety having from 1 to 6 carbon atoms, including for example, methyl, ethyl, n- propyl, isopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, n-pentyl and n-hexyl.

As used herein the term"divalent (Ci-Cg) alkylene radical"means a saturated hydrocarbon chain having from 1 to 6 carbon atoms and two unsatisfied valences.

As used herein the term" (C2-CÔ) alkenyl"means a straight or branched chain alkenyl moiety having from 2 to 6 carbon atoms having at least one double bond of either E or Z stereochemistry where applicable. The term includes, for example, vinyl, allyl, 1-and 2-butenyl and 2-methyl-2-propenyl.

As used herein the term"divalent (C2-Cs) alkenylene radical"means a hydrocarbon chain having from 2 to 6 carbon atoms, at least one double bond, and two unsatisfied valences.

As used herein the term"C2-C6 alkynyl"refers to straight chain or branched chain hydrocarbon groups having from two to six carbon atoms and having in addition one triple bond. This term would include for example, ethynyl, 1-propynyl, 1-and 2- butynyl, 2-methyl-2-propynyl, 2-pentynyl, 3-pentynyl, 4-pentynyl, 2-hexynyl, 3- hexynyl, 4-hexynyl and 5-hexynyl.

As used herein the term"divalent (C2-C6) alkynylene radical"means a hydrocarbon chain having from 2 to 6 carbon atoms, at least one triple bond, and two unsatisfied valences.

As used herein the term"cycloalkyl"means a saturated alicyclic moiety having from 3-8 carbon atoms and includes, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

As used herein the term"cycloalkenyl"means an unsaturated alicyclic moiety having from 3-8 carbon atoms and includes, for example, cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl and cyclooctenyl. In the case of cycloalkenyl rings of from 5-8 carbon atoms, the ring may contain more than one double bond.

As used herein the term"aryl"refers to a mono-, bi-or tri-cyclic carbocyclic aromatic group, and to groups consisting of two covalently linked monocyclic carbocyclic aromatic groups. Illustrative of such groups are phenyl, biphenyl and napthyl.

As used herein the unqualified term"heterocyclyl"or"heterocyclic"includes "heteroaryl"as defined below, and in particular means a 5-8 membered aromatic or non-aromatic heterocyclic ring containing one or more heteroatoms selected from S, N and O, and optionally fused to a benzyl or second

heterocyclic ring, and the term includes, for example, pyrrolyl, furyl, thienyl, piperidinyl, imidazolyl, oxazolyl, thiazolyl, thiadiazolyl, thiazepinyl, pyrazolyl, pyridinyl, pyrrolidinyl, pyrimidinyl, morpholinyl, piperazinyl, indolyl, and benzimidazolyl rings.

As used herein the term"heteroaryl"refers to a 5-or 6-membered aromatic ring containing one or more heteroatoms, and optionally fused to a benzyl or pyridyl ring; . and to groups consisting of two covalently linked 5-or 6-membered aromatic rings each containing one or more heteroatoms; and to groups consisting of a monocyclic carbocyclic aromatic group covalently linked to a 5-or 6-membered aromatic rings containing one or more heteroatoms. Illustrative of such groups are thienyl, furyl, pyrrolyl, imidazolyl, benzimidazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, 4- ( [1,2,3]-thiadiazoly-4-yl) phenyl and 5-isoxazol-3-ylthienyl.

As used herein the unqualified term"carbocyclyl"or"carbocyclic"refers to a 5-8 membered ring whose ring atoms are all carbon.

Unless otherwise specified in the context in which it occurs, the term"substituted"as applied to any moiety herein means substituted with up to four substituents, each of which independently may be (C,-C6) alkyl, phenyl, benzyl, (C,-C6) alkoxy, phenoxy, hydroxy, mercapto, (Ci-Ce) alkylthio, amino, halo (including fluoro, chloro, bromo and iodo), trifluoromethyl, cyano, nitro, oxo,-COOH,-CONH2,-COR A,-COORAI_ NHCORA,-CONHRA,-NHRA,-NRARe, or-CONRARB wherein RA and RB are independently a (C,-C6) alkyl group. In the case where"substituted"means substituted by benzyl, the phenyl ring thereof may itself be substituted with any of the foregoing, except phenyl or benzyl.

As used herein the terms"side chain of a natural alpha-amino acid"and"side chain of a non-natural alpha-amino acid"mean the group Rx in respectively a natural and non-natural amino acid of formula NH2-CH (R')-COOH.

Examples of side chains of natural alpha amino acids include those of alanine, arginine, asparagine, aspartic acid, cysteine, cystine, glutamic acid, histidine, 5- hydroxylysine, 4-hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, a-aminoadipic acid, a-amino-n-butyric acid, 3,4-dihydroxyphenylalanine, homoserine, a- methylserine, ornithine, pipecolic acid, and thyroxine.

In natural alpha-amino acid side chains which contain functional substituents, for example amino, carboxyl, hydroxy, mercapto, guanidyl, imidazolyl, or indolyl groups as in arginine, lysine, glutamic acid, aspartic acid, tryptophan, histidine, serine, threonine, tyrosine, and cysteine, such functional substituents may optionally be protected.

Likewise, in the side chains of non-natural alpha amino acids which contain functional substituents, for example amino, carboxyl, hydroxy, mercapto, guanidyl, imidazolyl, or indolyl groups, such functional substituents may optionally be protected.

The term"protected"when used in relation to a functional substituent in a side chain of a natural or non-natural alpha-amino acid means a derivative of such a substituent which is substantially non-functional. The widely used handbook by T. W.

Greene and P. G. Wuts"Protective Groups in Organic Synthesis"Second Edition, Wiley, New York, 1991 reviews the subject. For example, carboxyl groups may be esterified (for example as a Ci-Cg a) ky) ester), amino groups may be converted to amides (for example as a NHCOC,-C6 alkyl amide) or

carbamates (for example as an NHC (=O) OC1-C6 alkyl or NHC (=O) OCH2Ph carbamate), hydroxyl groups may be converted to ethers (for example an OC1-C6 alkyl or a O (C,-C6 alkyl) phenyl ether) or esters (for example a OC (=O) Ci-Cg alkyl ester) and thiol groups may be converted to thioethers (for example a tert-butyl or benzyl thioether) or thioesters (for example a SC (=O) Ci-Cg alkyl thioester).

There are at least two actual or potential chiral centres in the compounds according to the invention because of the presence of asymmetric carbon atoms. The presence of several asymmetric carbon atoms gives rise to a number of diastereoisomers with R or S stereochemistry at each chiral centre. The invention includes all such diastereoisomers and mixtures thereof. Currently, the preferred stereoconfiguration of the carbon atom carrying the R2 group is R; that of the carbon . atom carrying the R, group (when asymmetric) is R; and that of the carbon atom carrying the R3 group (when asymmetric) is S In the compounds of formula (I) as defined above: R, is hydrogen, methyl, or trifuoromethyl. Hydrogen is currently preferred.

R2 may be, for example: optionally substituted Cl-C. alkyl, C3-C6 alkenyl, C3-C6 alkynyl or cycloalkyl; phenyl (C,-C6 alkyl)-, phenyl (C3-C6 alkenyl)-or phenyl (C3-C6 alkynyl)- optionally substituted in the phenyl ring; cycloalkyl (C,-C6 alkyl)-, cycloalkyl (C3-Cs alkenyl)-or cycloalkyl (C3-C6 alkynyl)- optionally substituted in the cycloalkyl ring; heterocyclyl (C,-C6 alkyl)-, heterocyclyl (C3-C6 alkenyl)-or heterocyclyl (C3-C6 alkynyl)-optionally substituted in the heterocyclyl ring; or CH3 (CH2) pO (CH2) or CH3 (CH2) pS (CH2) q-, wherein p is 0,1,2 or 3 and q is 1, 2 or 3.

Specific examples of R2 groups inciude methyl, ethyl, n-and iso-propyl, n-and iso-butyl, n-pentyl, iso-pentyl 3-methyl- but-1-yl, n-hexyl, n-heptyl, n-acetyl, n-octyl, methylsulfanylethyl, 2-ethoxyethyl,2-ethoxymethyl,3-ethylsulfanylmethyl,2-methoxyethyl, hydroxypropyl, allyl, 3-phenylprop-3-en-1-yl, prop-2-yn-1-yl, 3-phenylprop-2- yn-1-yl, 3-(2-chlorophenyl) prop-2-yn-1-yl, but-2-yn-1-yl, cyclopentyl, cyclohexyl, cyclopentylpropyl,cyclopentylethyl, cyclohexylpropyl,furan-2-ylmethyl,furan-3-cyclohexylmethyl,cyclohexylethyl, <BR> <BR> <BR> methyl, tetrahydrofuran-2-ylmethyl, tetrahydrofuran-2-ylmethyl,<BR> <BR> <BR> <BR> <BR> piperidinyimethyl, phenylpropyl, 4-chlorophenylpropyl, 4-methylphenylpropyl, 4-methoxyphenylpropyt, benzyl, 4-chlorobenzyl, 4-methylbenzyl, and 4- methoxybenzyl.

Presently preferred groups at R2 are n-propyi, n-butyl, n-pentyi, and cyclopentylmethyl.

R3 may be, for example the characterising group of a natural a amino acid, for example benzyl, or 4-methoxyphenylmethyl, in which any functional group may be protected, any amino group may be acylated and any carboxyl group present may be amidated; or a group- [Alk] nRg where Alk is a (C,-C6) alkylene or (C2-C6) alkenylene group optionally interrupted by one or more -O-, or-S-atoms or-N (R, 2)-groups [where R12 is a hydrogen atom or a (Cl-C6) alkyl group], n is 0 or 1, and Rg is hydrogen or an optionally substituted phenyl, aryl, heterocyclyl, cycloalkyl or cycloalkenyl group or (only when n is 1) Rg may additionally be hydroxy, mercapto, (C,-C6) alkylthio, amino, halo, trifluoromethyl, nitro,-COOH,- -NHCORA,-CONHRA,-NHRA,-NRARB,or-CONRARBCONH2,-COORA, wherein RA and RB are independently a (C,-C6) alkyl group; or -NHCORA,-CONHRA,-NHRA,-NRARB,or-CONRARBCONH2,-COORA, wherein RA and RI are independently a (C,-C6) alkyl group; or a benzyl group substituted in the phenyl ring by a group of formula- OCH2CORs where R8 is hydroxyl, amino, (C1-C6) alkoxy, phenyl(C1-C6)alkoxy, (C,-C6) alkylamino, di ( (C,-C6) alkyl) amino, phenyl (C,-C6) alkylamino; or a heterocyclic (C,-C6) alkyl group, either being unsubstituted or mono-or di- substituted in the heterocyclic ring with halo, nitro, carboxy, (Ci-Ce) alkoxy, cyano, (C,-C6) alkanoyl, trifluoromethyl (C1-C6)alkyl, hydroxy, formyl, amino, mercapto,(C1-C6)alkylthio,(C1-C6) alkylamino,di-(C1-C6)alkylamino, hydroxy (C,-C6) alkyl, mercapto (C,-C6) alkyl or (C,-C6) alkylphenylmethyl; or a group-CRaRbRC in which: each of Ras Rb and Rc is independently hydrogen, (C,-C6) alkyl, (C2- C6) alkenyl, (C2-C6) alkynyl, phenyl (C,-C6) alkyl, (C3-C8) cycloalkyi; or Ré is

hydrogen and Ra and Rb are independently phenyl or heteroaryl such as pyridyl; or Rc is hydrogen, (Ci-Ce) alkyl, (C2-C6) alkenyl, (C2-C6) alkynyl, phenyl (C,- C6) alkyl, or (C3-C8) cycloalkyl, and Ra and Rb together with the carbon atom to which they are attached form a 3 to 8 membered cycloalkyl or a 5- to 6-membered heterocyclic ring; or Ra, Rb and Ré together with the carbon atom to which they are attached form a tricyclic ring (for example adamantyl); or Ra and Rb are each independently (Ci-Ce) alkyl, (C2-C6)alkenyl, (C2- C6) alkynyl, phenyl (C,-C6) alkyl, or a group as defined for Rc below other hydrogen,-OH,-SH, halogen,-CN,-CO2H, (C,-C4) perfluoroalkyl,- -O(C1-C6)alkyl,-O(C2-C6)alkenyl,-S(C1-CH2OH,-CO2(C1-C6)alkyl, -SO2(C1-C6)alkyl,-S(C2-C6)alkenyl,-SO(C2-C6)alkyl,-SO(C1-C6) alkyl, C6) alkenyl,-SO2 (C2-C6) alkenyl or a group-Q-W wherein Q represents a bond or-O-,-S-,-SO- or-SO2-and W represents a phenyl, phenylalkyl, (C3-C8) cycloalkyl, (C3-C8) cycloalkylalkyl, (C4- C8) cycioalkenyi, (C4-Ce) cycloalkenylalkyl, heteroaryl or heteroarylalkyl group, which group W may optionaily be substituted by one or more substituents independently selected from, hydroxyl, halogen,-CN,- CO2H,-CO2 (C,-C6) alkyl,-CONH2,-CONH (C,-C6) aikyl,-CONH (C,- -CH2OH,(C1-C4) perfluoroalkyl,-O(C1-C6)alkyl,-S(C1-C6alkyl)2,-CHO, C6)aikyl,-SO (C,-C6) alkyl,-SO2 (C,-C6) alkyl,-NO2,-NH2,-NH (C,-C6) alkyl, -N ((C1-C6) alkyl) 2,-NHCO (C,-C6) alkyl, (C,-C6) alkyl, (C2-C6) alkenyl, (C2- C6) alkynyl, (C3-C8) cycloalkyl, (C4-C8) cycloalkenyl, phenyl or benzyl.

Examples of particular R3 groups include methyl, ethyl, benzyl, 4- chlorobenzyl, 4-hydroxybenzyl, phenyl, cyclohexyl, cyclohexylmethyl, pyridin- 3-ylmethyl, tert-butoxymethyl, naphthylmethyl, iso-butyl, sec-butyl, tert-butyl, 1-benzylthio-1-methylethyl, 1-methylthio-1-methylethyl, 1-mercapto-1-<BR> methylethyl, 1-methoxy-1-methylethyl, 1-hyd roxy-1-methylethyl, 1-fluoro-1- methylethyl, hydroxymethyl, 2-hydroxethyl, 2-carboxyethyl, 2- methylcarbamoylethyl, 2-carbamoylethyl, and 4-aminobutyl. Presently preferred R3 groups include tert-butyl.

R4 may be, for example optionally substituted C,-C8 alkyl, C2-C6 alkenyl, C2-C6 alkynyl or cycloalkyl; optionally substituted phenyl, biphenyl or naphthyl; optionally substituted piperidinyl, cyclohexyl, cyclopentyl, oxazolyl, thiazepinyl, pyridinyl, pyrrolidinyl, pyrimidinyl, morpholinyl, piperazinyl, indolyl, optionally substituted piperidinyl, cyclohexyl, cyclopentyl, oxazolyl, thiazepinyl, pyridinyl, pyrrolidinyl, pyrimidinyl, morpholinyl, piperazinyl, indolyl, thienyl, furanyl, pyrrolyl, imidazolyl, benzofuranyl, benzothienyl, benzimidazolyl, thiazolyl, benzothiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyridazinyl, pyrazinyl, or triazinyl. phenyl (C,-C6 alkyl)-, phenyl (C2-C6 alkenyl)-or phenyl (C2-C6 alkynyl)- optionally substituted in the phenyl ring; cycloalkyl (C,-C6 alkyl)-, cycloalkyl (C2-C6 alkenyl)-or cycloalkyl (C2-C6 alkynyl)- optionally substituted in the cycloalkyl ring; heterocyclyl (C,-C6 alkyl)-, heterocyclyl (C2-C6 alkenyl)-or heterocyclyl (C2-C6 alkynyl)-optionally substituted in the heterocyclyl ring.

Specific examples of R4 groups include Methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 2-phenylcycloprop-1-yl, benzyl, biphenyl-2-yl, biphenyl-3-yl, biphenyl-4-yl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2,3- dimethoxyphenyl, 2,4-dimethoxyphenyl, 3,4-dimethoxyphenyl, 2- phenoxyphenyl, 3-phenoxyphenyl, 4-phenoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2-bromophenyl, 3-bromophenyl, 4- bromophenyl, 2-iodophenyl, 3-iodophenyl, 4-iodophenyl, 2-methylphenyl, 3- methytphenyl, 4-methylphenyl, 3,4-dimethyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-acetamidophenyl, 3-acetamidophenyl, 4-acetamidophenyl, 2-N, N-dimethylaminophenyl, 3-N, N-dimethylaminophenyl, 4-N, N- dimethylaminophenyl, 2-methanesulfonamidophenyl, 3- methanesulfonamidophenyl, 4-methanesulfonamidophenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4- dihydroxyphenyl, 3-thiophenolyl,4-2-thiophenolyl, thiophenolyl, 2-thioanisolyl, 3-thioanisolyl, 4-thioanisolyl, 1-naphthyl, 2-naphthyl, furan-2-yl, thien-2-yl, pyrrol-2-yl, 1-methylpyrrol-2-yl, imidazol-2-yl, 5-phenylpyrrol-2-yl,5-phenylfuran-2-yl,5-1-methylimdiazol-2-yl,thiazol-2-yl, phenylthien-2-yl, benzothiazol-2-yl, 1, 2,4-oxadiazol-5-yl, 3-methyl-1,2,4- oxadiazol-5-yl, 3-phenyl-1,2,4-oxadiazol-5-yl, 1,2,4-oxadiazol-3-yl,

1,3,4- oxadiazol-2-yl, 1,2,4-thiadiazol-5-yl, 1,3,4-thiadiazol-2-yl, pyridin-2-yl, pyridin- 3-yl, pyridin-4-yl, N-oxides of pyridin-2-yl pyridin-3-yl and pyridin-4-yl, indol-2- yl, indol-3-yl, 1-methylindol-2-yl, 1-methylindol-3-yl, benzimidazol-2-yl, 1- methylbenzimidazol-2-yl, pyrazin-2-yl, 1,2-pyridazin-3-yl, 1,3-pyrimidin-2-yl, benzo [b] thien-2-yl, benzo[b]thien-3-yl, benzo [b] furan-2-yl, benzo [b] furan-3-yl, isoxazol-5-yl, quinolin-2-yl, quinolin-3-yl, isoquinolin-2-yl, isoquinolin-3-yl, 2- oxo-2-phenylethyl, diphenylmethyl, 4-N-methylaminophenyl, 4-N, N- dimethylcarboxamidophenyl, and 4-carboxyphenyl. R4 may be a phenyl group which is substituted, for example in the 4-position, by one of the following: In the compounds of formula (I) as defined above wherein Z is a radical of formula- C (=O) NH (OH) the radicals Ri, Rs, Rs, R4 may be any of those discussed above in relation to compounds (I) wherein Z is a radical of formula-N (OH) CH (=O). However, in addition, R, may be, for example, a hydroxy, methoxy, ethoxy, n-propyioxy, allyloxy, amino, methylamino, dimethylamino, ethylamino, or diethylamino group.

Specific examples of compounds of the invention include those disclosed in the Examples herein.

Compounds of the invention wherein Z is a radical of formula-N (OH) CH (=O) may be prepared by N-formylation of a compound of formula (II) wherein-OP represents a protected hydroxy group, and R,, R2, R3 and R4 are as defined in relation to formula (I) except that any reactive groups present therein which are reactive with the formylation reagent are protected, and then converting- OP to a hydroxy group and removing any protecting groups present in R"R2, R3 or R4. Formylacetic anhydride is a convenient formylating agent for this reaction.

. Compounds of formula (I I) may be synthesised from easily accessible or commercially available starting materials, or by standard synthetic routes analogous to those shown in Schemes 1 and 2 below.

Hydroxamate compounds of formula (I) for use in accordance with the invention may be prepared by reacting the parent compound wherein Z is a carboxylic acid group with hydroxylamine or an N-and/or O-protected hydroxylamine, and thereafter removing any O-or N-protecting groups.

Antibacterial or antiprotozoal compositions with which the invention is concerned may be prepared for administration by any route consistent with the pharmacokinetic properties of the active ingredient (s).

Orally administrable compositions may be in the form of tablets, capsules, powders, granules, lozenges, liquid or gel preparations, such as oral, topical, or sterile parenteral solutions or suspensions. Tablets and capsules for oral administration may be in unit dose presentation form, and may contain conventional excipients such as binding agents, for example syrup, acacia, gelatin, sorbitol, tragacanth, or polyvinyl-pyrrolidone; fillers for example lactose, sugar, maize-starch, calcium phosphate, sorbitol or glycine; tabletting lubricant, for example magnesium stearate, talc, polyethylene glycol or silica; disintegrants for example potato starch, or acceptable wetting agents such as sodium lauryl sulphate. The tablets may be coated according to methods well known in normal pharmaceutical practice. Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, mulsions, syrups or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, glucose syrup, gelatin hydrogenated edible fats; emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example almond oil, fractionated coconut oil, oily esters such as glycerine, propylene glycol, or ethyl aicohol ; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid, and if desired conventional flavouring or colouring agents.

For topical application to the skin, the active ingredient (s) may be made up into a cream, lotion or

ointment. Cream or ointment formulations which may be used for the drug are conventional formulations well known in the art, for example as described in standard textbooks of pharmaceutics such as the British Pharmacopoeia.

The active ingredient (s) may also be administered parenterally in a sterile medium.

Depending on the vehicle and concentration used, the drug can either be suspended or dissolved in the vehicle. Advantageously, adjuvants such as a local anaesthetic, preservative and buffering agents can be dissolved in the vehicle. Intra-venous infusion is another route of administration for the compounds used in accordance with the invention.

Safe and effective dosages for different classes of patient and for different disease states will be determined by clinical trial as is required in the art. It will be understood that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

The following example illustrate embodiments of the invention.

The following abbreviations have been used throughout: CDI 1,1'-Carbonyldiimidazole DMF N, N-Dimethylformamide EDC N-Ethyl-N'- (3-dimethylaminopropyl) carbodiimide hydrochloride TFA Trifluoroacetic acid HOBt 1-Hydroxybenzotriazole HPLC High performance liquid chromatography LRMS Low solution mass spectrometry THF Tetrahydrofuran TLC Thin layer chromatography 'H and 13C NMR spectra were recorded using a Bruker AC 250E spectrometer at 250.1 and 62.9 MHz, respectively. Mass spectra were obtained using a Perkin Elmer Sciex API 165 spectrometer using both positive and negative ion modes.

Where MIC values are quoted for the compounds of the examples, those results were obtained by the method described in the Biological Example.

Example 1 2(R)-[(N-Formyl-N-hyd roxya mino)-methyl]-hexanoic acid-(1'(S)-(4-fl uorobenzoyl)- 2', 2'-dimethylpropyl) amide.

The title compound was prepared as described in Scheme 1. The experimental details of the synthesis and relevant spectroscopic data are described below.

Scheme 1 Step A 0 Step B 0 OMe OH OH N HZNp'N OFiJ'N N\ I H I H I O O F F O Step C 0 Step D F Step E ,o N H2N H O p NH OBn 0 F F Step F Step G 0 Hw Ht O H N-OBn O ; H OAH Reagents and Conditions: A. Di-tert-butyidicarbamate, Et3N, MeOH B. HN (OMe) Me. HCI, CDI, CH2C12 C. 4-Fluorophenylmagnesium bromide, THF, 0 oC to 25 oc, 20 hours D. TFA, CH2Cl2, <5 oC, 16 hours E. 2 (R)- (Benzyloxy-amino-methyl)-hexanoic acid, WSC, 10 mol% HOBT, DMF, 16 hours F. Formylacetic anhydride, CH2Cl2, RT, 1 hour G. H2, 10% Pd/C, EtOAc/MeOH STEP A: 2 (S)-tert-Butoxycarbonylamino-3,3-dimethyi-butyric acid To a suspension of L-tert-leucine (26.1 g, 0.2 mol) in methanol (150 mL) was added triethylamine (56 mL, 0.4 mol) and the mixture cooled to 0 °C. To the mixture was added slowly a solution of di-tert-butyldicarbamate (48 g, 0.22 mol) in methanol (40 mL) such that an internal temperature of between 0 and 5 °C was maintained. The reaction was allowed to stir overnight and the solvents were removed in vacuo. The residue was dissolved in ethyl acetate (200 mL) and washed with 10% w/v aqueous citric acid solution (3 x 100 mL). The organic layer was dried over MgSO4, filtered and the solvents removed in vacuo to give the title product as a pale yellow oil

(48.9 . g, >100 %, residual solvent).

'H NMR (CDCI3): b/ppm 9.20 (1H, bs), 5.10 (1H, m), 4.15 (1H, m), 1.45 (9H, s), 1.00 (9H, s).

STEP B: [1 (S)- (Methoxy-methyl-carbamoyl)-2, 2-dimethylpropyl]-carbamic acid-tert- butyl ester.

To a solution of 2 (S)-tert-butoxycarbonylamino-3, 3-dimethyl-butyric acid (30 g, 0.13 mol) in dichloromethane (400 mL) was added portionwise 1,1'-carbonyidiimidazole (63.3 g, 0.39 mol). After addition was complete the reaction was allowed to stir for 15 minutes before N-methoxy-N-methylamine hydrochloride (38 g, 0.39 mol) was added and the reaction allowed to stir for 16 hours. The solvents were removed in vacuo and the residue partitioned between ethyl acetate (250 mL) and 1 M HCI (150 mL).

The organic phase was washed with 1 M HCI solution (2 x 100 mL), saturated sodium bicarbonate solution (2 x 100 mL) and brine (100 mL). The organic phase was dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil. Purification by column chromatography (SiO2,30% ethyl acetate in hexanes) afforded the title product as a pale yellow oil (26.5 g, 74 %).

'H NMR (CDC13): #/ppm 5.20 (1H, bd, J = 9.5 Hz), 4.65 (1H, d, J = 10.4 Hz), 3.77 (3H, s), 3.21 (3H, s), 1.43 (9H, s), 0.97 (9H, s).

LRMS: (m/z) 297 (M+Na) +.

STEP C: (1 (S)- (4-Fluorobenzoyl) 1-2, 2-dimethylpropyl) carbamic acid-tert-butyl ester [1 (S)-(Methoxy-methyl-carbamoyl)-2, 2-dimethylpropyl]-carbamic acid-tert-butyl ester (548 mg, 2.0 mmol) was dissolved in freshly distilled THF (10 mL) under an argon atmosphere. The solution was cooled to 0 °C whereupon 4-fluorophenylmagnesium bromide (8.0 mL, 1.0 M in THF, 8.0 mmol, 4 eqv) was added dropwise maintaining an internal temperature < 5 °C. The reaction was stirred at 0 °C for 30 minutes before warming to room temperature for a further 20 hours. After this time the reaction was cooled to 0 °C and saturated aqueous ammonium chloride solution (30 mL) was added. The aqueous phase was extracted with ethyl acetate (3 x 30 mL) and the organic phases washed with water (3 x 50 mL) and brine (50 mL), dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (SiO2,20 % ethyl acetate in hexanes) afforded the title compound as a white solid (447 mg, 72%).

'H NMR (CDCI3): b/ppm 8.03 (2H, m), 7.14 (2H, t, J = 8.5 Hz), 5.41 (1H, bd, J = 9.6 Hz), 5.12 (1H, d, J=9. 6 Hz), 1.43 (9H, s), 0.92 (9H, s).

LRMS: (m/z) 332 (M+Na) +.

STEP D: 2 (S)-Amino-1- (4-fluorophenyl)-3, 3-dimethyl-butan-1-one.

To a solution of (1 (S)- (4-fluorobenzoyl) 1-2, 2-dimethylpropyl) carbamic acid-tert-butyl ester (319 mg, 1.03 mmol) in dichloromethane (5 mL) at 0 °C was added trifluoroacetic acid (2 mL). The reaction was placed at <5 °C for 16 hours before the solvents were removed in vacuo to give a bright yellow oil. The residue was dissolved in methanol (30 mL) and was treated portionwise with Dowex 1X8-400 basic resin until pH 9. Filtration and removal of the solvents in vacuo gave the title compound as a pale yellow oil (-1.0 g, > 100 %, residual water). Purification by column chromatography (Si02,5 % methanol in dichloromethane) gave the title compound as a colourless oil (190 mg, 88 %).

'H NMR (CDCt,): b/ppm 8.10 (2H, m), 7.15 (2H, t, J = 8.4 Hz), 4.20 (1H, s), 1.70 (2H, bs), 0.93 (9H, s).

LRMS: (m/z) 210 (M+H)'.

STEP E: 2 (R)-(N-Benzyloxyaminomethyl)-hexanoic acid-(1'(S)-(4-fluorobenzoyl)- 2', 2'-dimethylpropyl) amide . To a suspension of 2 (R)- (N-benzyloxyamino-methyl)-hexanoic acid (237 mg, 0.91 mmol, 1.1 eqv) in DMF (5 mL) at 0 °C was added EDC (200 mg, 1.1 eqv) and 1-hydroxybenzotriazole (12 mg, 10 mol%). The mixture was allowed to stir at 0 °C for 45 minutes before a solution of 2 (S)-amino-1- (4-fluorophenyl)-3, 3-dimethyl-butan-1- one (179 mg, 0.83 mmol, 1 eqv) in DMF (2 mL) was added. The reaction was allowed to warm to room temperature and stirred for 16 hours. The solvents were removed in vacuo and the residue dissolved in ethyl acetate (30 mL) and 10% w/v aqueous citric acid (40 mL). The aqueous phase was extracted with ethyl acetate (3 x 20 mL) and the combined organic layers washed with saturated sodium hydrogen carbonate (70 mL) and brine (2 x 70 mL). The organic phases were dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (SiO2,30 % ethyl acetate in hexanes) gave the title compound as a clear oil (160 mg, 42 %).

'H NMR (CDCI3): b/ppm 8.07 (2H, m), 7.35 (5H, m), 7.13 (2H, t, J = 8.7 Hz), 6.99 (1H, d, J = 9.0 Hz), 5.52 (1 H, d, J = 9.0 Hz), 4.75 (2H, s), 3.10 (2H, m), 2.52 (1H, m), 1.70-1.10 (6H, m), 0.94 (9H, s), 0.81 (3H, t, J = 6.6 Hz).

LRMS: (m/z) 443 (M+H) + STEP F: 2 (R)- [N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(1' (S)- (4- fluorobenzoyl)-2', 2'-dimethylpropyl) amide.

To a solution of 2 (R)- (N-benzyloxyaminomethyl)-hexanoic acid- (1' (S)- (4- fluorobenzoyl)-2', 2'-dimethylpropyl) amide (150 mg, 0.35 mmol) in dichloromethane (10 mL) at 0 °C was added formylacetic anhydride (80 slL, 0.88 mmol, 2.5 eqv) and the reaction allowed to stir at room temperature. After 2 hours the solvents were removed in vacuo and the residue azeotroped with toluene (3 x 30 mL). The product was placed under high vacuum to give the title compound as a pale yellow solid (145 mg, 88 %).

'H NMR (CDCI,): 5/ppm 8.20-7.85 (3H, bm), 7.40 (5H, m), 7.15 (2H, m), 6.31 (1 H, d, J = 9.3 Hz), 5.42 (1 H, d, J = 9.2 Hz), 5.10-4.70 (2H, bm), 3.90-3.60 (2H, bm), 2.58 (1 H, m), 1.80-1.05 (6H, m), 0.89 (9H, s), 0.78 (3H, t, J = 6.8 Hz).

LRMS: (m/z) 471 (M+H) +.

STEP G: 2 (R)- [N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (1' (S)- (4- fluorobenzoyl)-2', 2'-dimethylpropyl) amide To a solution 2 (R)- [N-benzyloxy-N-formylamino)-methyl]-hexanoic acid-(l' (S)- (4- fluorobenzoyl)-2', 2'-dimethylpropyl) amide (145 mg, 0.31 mmol) in methanol (10 mL) under an argon atmosphere was added a slurry of 10% Pd/C (15 mg) in ethyl acetate (1 mL). Hydrogen gas was bubbled through the reaction for 15 minutes after which time the reaction was allowed to stir under 1 atmosphere of hydrogen for two hours. The reaction was flushed with argon and filtered through glass wool. The solvents were removed in vacuo to afford the title compound as a hygroscopic white crystalline solid (105 mg, 90%).

'H NMR (CDC ! s): b/ppm 8.40 (0.3H, s), 8.05 (2H, dd, J = 6.8,5.4Hz), 7.86 (0.7H, s), 7.16 (2H, t, J = 3.2Hz), 6.90 (0.3H, bd, J = 9. 1 Hz), 6.82 (0.7H, bd, J = 9.2Hz), 5.50 (1H, d, J = 9.3Hz), 4.02 (0.2H, dd,

J = 14.5,7.5Hz), 3.87 (0.8H, dd, J = 14.2, 10. 0Hz), 3.62 (0.2H, dd, J = 11.0,3.0Hz), 3.46 (0.8H, dd, J = 14.1,4.6Hz), 2.88- 2.70 (1H, m), 1.55 (1 H, m), 1.45-1. 10 (5H, m), 0.94 (2H, s), 0.90 (7H, s), 0.78 (3H, t, J = 6.6Hz).

"C NMR (CDC13): b/ppm 5,164.5,134.5,131.8,131.7, 4,48.1,45.0,35.7,30.5,29.8,29.5, 5,27.4,22.9,14.2.

LRMS: (m/z) 381 (M+H) +, 403 (M+Na) +.

MIC (E. Col/): 12. 5 µM MIC (S. Capitis): 25 1M Example 2 2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4-methoxybenzoyl 2', 2'dimethylpropyl) amide The title compound was prepared as described in Scheme 1 in an analogous manner to 2 (R)- [N-formyl-N-hydroxyamino)-methyl]-hexanoic acid- (1' (S)- (4- fluorobenzoyl)-2', 2'-dimethylpropyl) amide. The relevant spectroscopic data are described below.

STEP C: (1 (S)-(4-Methoxybenzoyl)1-2,2-dimethylpropyl) carbamic acid-tert-butyl ester Purification by column chromatography (SiO2,20 % ethyl acetate in hexanes) afforded the title compound as a white solid (836 mg, 71%).

'H NMR (CDCI3): b/ppm 8.00 (2H, d, J = 8.8 Hz), 6.95 (2H, d, J = 8.8 Hz), 5.45 (1H. d, J = 9.5 Hz), 5.12 (1H, d, J = 9.8 Hz), 3.89 (3H, s), 1.43 (9H, s), 0.93 (9H, s).

STEP D: 2 (S)-Amino-1- (4-methoxyphenyl)-3, 3-dimethyl-butan-1-one.

Purification by column chromatography (SiO2,5 % methanol in dichloromethane) gave the title compound as a colourless oil (176 mg, 78 %).

1H NMR (CDCl3) : 6/ppm 7.95 (2H, d, J = 9. 0 Hz), 6.93 (2H, d, J = 9. 0 Hz), 4.20 (1 H, s), 3.89 (3H, s), 1.68 (2H, bs), 0.94 (9H, s).

LRMS: (m/z) 222 (M+H) +.

STEP E: 2 (R)- (N-Benzyloxyaminomethyl)-hexanoic acid- (1' (S)- (4-methoxybenzoyl)- 2', 2'-dimethylpropyl) amide Purification by column chromatography (SiO2,30 % ethyl acetate in hexanes) gave the title compound as a clear oil (215 mg, 61 %).

'H NMR (CDCl3) : b/ppm 8.01 (2H, d, J = 9.0 Hz), 7.35 (5H, m), 6.95 (2H, d, J = 9.0 Hz), 5.55 (1 H, d, J = 9.5 Hz), 4.73 (2H, m), 3.87 (3H, s), 3.10 (2H, m), 2.51 (1 H, m), 1.70-1.10 (6H, m), 0.94 (9H, s), 0.80 (3H, t, J = 6.7 Hz).

LRMS: (m/z) 455 (M+H) + STEP F: 2 (R)- [N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(l' (S)- (4- <BR> <BR> <BR> <BR> methoxybenzoyl)-2', 2'-dimethylpropyl) amide<BR> <BR> <BR> <BR> <BR> <BR> <BR> <BR> <BR> <BR> <BR> <BR> <BR> The title compound was isolated as a pale yellow solid (187 mg, 88 %).

'H NMR (CDCl3) : b/ppm 8.20-7.85 (3H, m), 7.60-7.30 (5H, m), 7.05-6. 90 (2H, bd, J = 8.7 Hz), 6.40 (1 H, bd, J = 9.2 Hz), 5.50 (1 H, bd, J = 9.3 Hz), 5.10-4.70 (2H, bm), 3.92 (3H, bs), 3.75 (2H, bm), 2.60 (1H, m), 1.90-1.10 (6H, m), 0.89 (9H, s), 0.77 (3H, m).

LRMS: (m/z) 483 (M+H) +.

STEP G: 2 (R)-[N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4- methoxybenzoyl)-2', 2'-dimethylpropyl) amide The title compound was isolated as a hygroscopic white crystalline solid (133 mg, 98%).

'H NMR (CDCI3): b/ppm 8.40 (0.3H, s), 8.00 (2H, d, J = 8.8Hz), 7.86 (0.7H, s), 6.95 (2H, d, J = 8.8Hz), 6.76 (1H, d, J = 9.3Hz), 5.52 (1H, d, J = 9.4Hz), 4.10 (1H, m), 3.88 (3H, s), 3.62 (0.3H, dd, J = 14.6,3.1 Hz), 3.47 (0.7H, dd, J = 14.0,4. 0Hz), 2.85 (0.7H, m), 2.72 (0.3H, m), 1.55 (1H, m), 1.45-1.10 (5H, m), 0.94 (3H, s), 0.90 (6H, s), 0.77 (3H, t, J = 6.6Hz).

'3C NMR (CDCI3): #/ppm 199.2,198.9,176.3,173.3,164.7,164.5,131.6,131.5, 130.7,114.7,114.4,59.3,59.0,55.9,52.5,48.3,46.5,45.1,36.1,35.9,30.4,30.3, 2.

LRMS: (m/z) 391 (M-H)- ; 393 (M+H) +, 415 (M+Na) +.

MIC (E. Colt): 12. 5 μM MIC (S. Capitis): 6.25, uM Example 3 2(R)-[N-formyl-N-hydroxyamino)-methyl]-hexanoicacid-(1'(S)- cyclohexanecarbonyl-2'-methyipropyl) amide The title compound was prepared in an analogous manner to that described in Scheme 1 utilising 2 (S)-tert-butoxycarbonylamino-3-methyl-butyric acid as the starting material in Step B. The relevant spectroscopic data are described below.

STEP B: [1 (S)- (Methoxy-methyl-carbamoyl)-2-methylpropyl]-carbamic acid-tert-butyl ester.

The title product was isolated as a pale yellow oil (14.7 g, 82 %).

'H NMR (CDCI3): b/ppm 5.13 (1H, m), 4.57 (1H, m), 3.77 (3H, s), 3.21 (3H, s), 1.99 (1 H, m), 1.44 (9H, s), 0.96 (3H, d, J = 6. 8 Hz), 0.90 (3H, d, J = 6. 8 Hz).

STEP C: (1 (S)- (Cyclohexanecarbonyl)-2-methylpropyl) carbamic acid-tert-butyl ester Purification by column chromatography (SiO2,25 % ethyl acetate in hexanes) afforded the title compound as a white solid (253 mg, 42%).

'H NMR (CDCl3) : #/ppm 5.13 (1H, bd, J = 8.5 Hz), 4.40 (1H, m), 2.52 (1 H, m), 2.13 (1 H, m), 2.00-1.60 (7H, m), 1.44 (9H, s), 1.25 (3H, m), 1.01 (3H, d, J = 6.9 Hz), 0.75 (3H, d, J = 6.9 Hz).

STEP D: 2 (S)-Amino-1-cyclohexyl-3-methyl-butan-1-one The title compound was isolated as colourless oil (158 mg, 98 %).

'H NMR (CDCl3) : o/ppm 3.49 (1H, d, J = 3.7 Hz), 2.55 (1 H, m), 2.12 (1 H, m), 1.95- 1.10 (10H, m), 1.03 (3H, d, J = 6. 9 Hz), 0.75 (3H, d, J = 6. 8 Hz).

STEP E: 2 (R)- (N-Benzyloxyaminomethyl)-hexanoic acid- (1' (S)-cyclohexanecarbonyl- 2'-methylpropyl) amide Purification by column chromatography (SiO2,25 % ethyl acetate in hexanes) gave the title compound as a clear oil (116 mg, 35 %).

'H NMR (CDCl3) : #/ppm 7.35 (5H, m), 6.49 (1 H, d, J = 8.9 Hz), 5.70 (1 H, bs), 4.78 (1H, dd, J = 8.9,4.7 Hz), 4.72 (2H, s), 3.08 (2H, m), 2.52 (2H, m), 2.15 (1H, m), 2.05 -1.10 (16H, m), 0.98 (3H, d, J = 6. 8 Hz), 0.86 (3H, t, J = 6. 9 Hz), 0.78 (3H, d, J = 6.8 Hz).

LRMS: (m/z) 417 (M+H) + STEP F: 2 (R)- [N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(1' (S)- cyclohexanecarbonyl-2'-methylpropyl) amide The title compound was isolated as a viscous oil

(105 mg, 99 %).

'H NMR (CDCI3): b/ppm 8.30-7.80 (1H, m), 7.40 (5H, m), 6.12 (1H, m), 5.15-4.60 (3H, m), 3.95-3.50 (2H, m), 3.10 (1H, m), 2.55 (2H, m), 1.10-2.30 (16H, m), 1.10 -0.60 (9H, m).

LRMS: (m/z) 445 (M+H) +, 467 (M+Na) +.

STEP G: 2 (R)-[N-formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)- cyclohexanecarbonyl-2'-methylpropyl)amide The title compound was isolated as a hygroscopic white crystalline solid (67 mg, 84 %).

'H NMR (CDCI3): b/ppm 8.37 (0.3H, s), 7.81 (0.7H, s), 6.69 (1H, d, J = 9. 0Hz), <BR> <BR> <BR> 4.74 (1 H, dd, J = 9.0,5. 0Hz), 4.00 (0.3H, dd, J = 14.6,7.6Hz), 3.84 (0.7H, dd, J = 14.0,9.8Hz), 3.59 (0.3H, dd, J = 14.5,3.4Hz), 3.43 (0.7H, dd, J = 14.1,3.7Hz), 2.83 (0.7H, m), 2.70 (0.3H, m), 2.50 (1H, m), 2.12 (1H, m), 2.00-1.10 (16H, m), 1.00-0.60 (9H, m).

'3C NMR (CD30D): b/ppm 3,52.9,49.5,49.3,48.5,30.7, 3,26.1,25.6,25.5,23.0,20.3,17.6,14. 3.

. LRMS: (m/z) 355 (M+H)+, 377 (M+Na) +.

MIC (E. Coli): 50 μM MIC (S. Capitis): 25 μM Example 4 <BR> <BR> <BR> <BR> <BR> 3-Cyclopentyl-2 (R)- [ (N-formyl-N-hydroxyamino)-methyl]-N- [1' (S)- (4-fluorobenzoyl)- 2',2'-dimethylpropyl] propionamide The title compound was prepared in an analogous manner to that described in Scheme 1 utilising 2 (R)- (benzyloxyamino-methyl)-3-cyclopentyl-propionic acid in Step E. Spectroscopic data are described below. Experimental details of the synthesis of 2 (R)-(benzyloxyamino-methyl)-3-cyclopentyl-propionic acid and relevant spectroscopic data are also presented.

STEP G: 3-Cyclopentyl-2 (R)-[(N-formyl0N-hydroixyamino)-methyl]-N-[1'(S)-(4- fluorobenzoyl)-2', 2'-dimethylpropyl] propionamide The title compound was isolated as a hygroscopic white crystalline solid (120 mg, 81 %).

'H NMR (CD30D): b/ppm 8.27 (0.3H, s), 8.10 (2H, m), 7.85 (0.7H, s), 7.23 (2H, t, J=8.7Hz), 5.47 (1H, m), 3.77 (1H, m), 3.58 (0.3H, dd, J=14.0,5.6Hz), 3.42 (0.7H, dd, J=145. 1,4.7Hz), 3.09 (0.7H, m), 2.93 (0.3H, m), 1.82-1.20 (9H, m), 1.15-0.80 (11H, m).

'3C NMR (CD. OD) : b/ppm 5,169.8,165.7,136.3,132.9,132.8,117.4, 8,26.4, 26.3.

LRMS: (m/z) 407 (M+H) +.

MIC (E. Coll): 3.1 M MIC (S. Capitis): 3.1 μM Example 5 3-Cyclopentyl-2(R)-[(N-formyl-N-hydroxyamino)methyl]-N-[1'(S)-(4- methoxybenzoyl)-2',2'-dimethylpropyl] propionamide The title compound was prepared in an analogous manner to that described in Scheme 1 utilising 2 (R)-(benzyloxyamino-methyl)-3-cyclopentyl-propionic acid in Step E. Spectroscopic data are described below.

STEP G: 3-Cyclopentyl-2 (R)- [ (N-formyl-N-hydroxyamino)-methyl]-N- [1' (S)- (4- methoxybenzoyl)-2', 2'-dimethylpropyl] propionamide The title compound was isolated as a hygroscopic white crystalline solid (173 mg, 96 %).

'H NMR (CD30D): 5/ppm 8.26 (0.4H, s), 8.01 (2H, d, J=9. OHz), 7.85 (0.6H, s), 7.01 (2H, d, J=9. OHz), 5.49 (1 H, bs), 3.87 (3H, s), 3.79 (1 H, m), 3.59 (0.4H, dd, J=11.7,5.6Hz), 3.41 (0.6H, dd, J=14.4,4.9Hz), 3.09 (0.6H, m), 2.92 (0.4H, m), 1.85-1.20 (9H, m), 1.15-0.80 (11 H, m).

'3C NMR (CD30D): b/ppm 4,166.0,132.5,132.3,115.4,60.6, 4,26.3.

LRMS: (m/z) 419 (M+H)'.

MIC (E. coli): 3.1 pM MIC (S. capitis): 1.6 μM Synthesis of 2 (R)- (benzyloxyamino-methyl)-3-cyclopentyl-propionic acid ou oxo NA Step 1 Xc Step 2 OH Step 3 , bol 72% quant. OH 67% Ber OH 0 0fez Step 4 Step 5 BZIO NHOBzl I c OH 83% 84% O OH Reagents and Conditions: 1: Tical4, trioxane, CH2CI2; 2: H202, LiOH; 3: H2NOBn, WSC, THF/H20; 4: Ph3P, DIAD, THF; 5: LiOH, THF/MeOH/H20.

Step 1: 4S-Benzyl-3- [3-cyclopentyl-2R-hydroxymethyl-propionyl]-oxazolidin-2-one To a stirred, cooled (0 °C) solution of 4S-benzyl- (3-cyclopentyl-propionyl)-oxazolidin- 2-one (21 g, 69.8 mmoi) in dichloromethane (350 ml) was added a solution of titanium tetrachloride (1 M in dichioromethane, 73.25 mi, 73.2 mmol), dropwise. The resulting yellowish slurry was stirred for 10 minutes at 0 °C, and then DIPEA (13.37 ml, 76.7 ml) was added dropwise to furnish a dark-red solution. The stirring was maintained for 1 h at 0 °C, and then a solution of s-trioxane (7.53 g, 83.7 mmol), in dichloromethane (70 ml) was added dropwise followed by the addition of a solution of titanium tetrachloride (1 M in dichloromethane, 73.25 ml, 73.2 mmol). The reaction mixture was then stirred for 4 h at 0 °C. Saturated aqueous ammonium chloride (250 ml) was added to the reaction mixture and the aqueous layer was extracted with addition dichloromethane (2x300 ml). The combined organic layers were washed with water (150 mi) and with brine (80 ml), dried over anhydrous magnesium sulfate, filtered and concentrated in vacuo to yield a yellow solid which on trituration with diethyl ether furnished a white solid (16.57 g, 72%).

'H NMR (CDC13): 5/ppm 7.38-7.22 (5H, m), 4.70 (1H, m), (2H, m), 3.99 (1 H, m), 3.96-3.75 (2H, m), 3.31 (1 H, dd, J = 13.4 & 3.3 Hz), 2.82 (1H, dd, J = 13.4 & 9.4 Hz), 2.24 (1 H, dd, J = 8.3 & 4.5 Hz), 2.81-1.30 (4H, m) and 1.13 (1H, m); '3C NMR (CDCI3): 5/ppm 0,127.4,66.2,64.2,55.7, 9,37.8,34.6,33.0,32.4 and 25.1.

Step 2: 3-Cyclopentyl-2R-hydroxymethyl-propionic acid To a stirred, cooled (0 °C) solution of 4S-Benzyl-3-[3-cyclopentyl-2R-hydroxymethyl- propionyl]-oxazolidin-2-one (16.05 g, 48.5 mmol) in THF-water (4: 1,250 ml) was added 27.5% aqueous hydrogen peroxide (24 ml, 194 mmol), followed by lithium hydroxide monohydrate (4.07 g, 97 mmol) in water (50 ml). After the reaction was complete (30 min), THF was removed in vacuo. The aqueous layer was extracted with dichloromethane (3x100 ml) and acidified to pH 2 with 4M hydrochloric acid.

The aqueous layer was extracted with diethyl ether (2x150 ml). The combined organic layers were washed with brine (60 ml), dried over anhydrous magnesium sulfate and filtered. The solvent was removed in vacuo to afford a yellow oil which was further purified by column chromatography (25% ethyl acetate in hexanes to 100% ethyl acetate) to furnish the title compound as an oil (8.3 g, quant.).

'H NMR (CDCI3): b/ppm 6.60-5.90 (1 H, br s), 3.80-3.78 (2H, m), 2.67 (1 H, m), 1.98- 1.40 (9H, m) and 1.20-0.98 (2H, m).

'3C NMR (CDC13): b/ppm 181.0,63.2,46.9,37.8,34.5,32.7,32.6,25.1 and 25.1.

Step 3: N-Benzyloxy-3-cyclopentyl-2R-hydroxymethyl-propionamide To a stirred, cooled (0 °C) mixture of 3-cyclopentyl-2R-hydroxymethyl-propionic acid (1.1 g, 6.4 mmol) in THF-water (4: 1,30 ml), was added O-benzylhydroxylamine. The pH of the resulting solution was adjusted to 4.5 by addition of 1 M hydrochloric acid, and then EDC (1.84 g, 9.6 mmol) was added in one portion. The resulting solution was stirred for 2.5 h at room temperature while controlling pH at 4.5 by addition of 1 M hydrochloric acid. After removal of the THF, the aqueous layer was extracted with ethyl acetate (3x40 ml) and the combined organic layers were washed with 10% citric acid (3x15 ml), 5% sodium hydrogen carbonate and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo to afford the title compound as a colourless crystalline solid (1.18 g, 67%). This compound was then used without any further purification.

'H NMR (CDC): o/ppm 8.14 (1 H, br s), 7.40-7.34 (5H, m), 4.94 (2H, br s), 3.76-3.66 (2H, m), 1.79-1.47 (11 H, m) and 1.17-0.97 (2H, m).

LRMS: +ve ion 278 [M+H], 555 [2M+H].

Step 4: N-Benzyloxy-3R-cyclopentylmethyl-azetidin-2-one To a stirred, cooled (0 °C) solution of N-Benzyloxy-3-cyclopentyl-2R-hydroxymethyl- propionamide (8.63 g, 31.1 mmol) and triphenylphosphine (9 g, 34.2 mmol) in dry THF (320 ml) was added DIAD (6.12 ml, 31.1 mmol), dropwise. The resulting solution was stirred at room temperature overnight. After removal of THF in vacuo, the residue was purified by column chromatography (hexanes: ethyl acetate, 5: 1 to 3: 1) to give the desired product as a white solid (6.7 g, 83%).

'H NMR (CDCI3): o/ppm 7.76-7.39 (5H, m), 4.94 (2H, br s), 3.36 (1 H, m), 2.96-2.80 (2H, m), 1.89-1.38 (9H, m) and 1.18-0.98 (2H, m).

"C NMR (CDC13): o/ppm 2, 33.1,32.9,25.5 and 25.3.

LRMS: +ve ion 260 [M+H], 519 [2M+H].

Step 5: 2R-(Benzyloxyamino-methyl)-3-cyclopentyl-propionic acid To a stirred, cooled (0 °C) solution of N-Benzyloxy-3R-cyclopentylmethyl-azetidin-2- one (6.7 g, 25.8 mmol) in THF-methanol (3: 1,100 ml) was added lithium hydroxide monohydrate (1.3 g, 31.0 mmol) in water (25 ml). The reaction mixture was stirred and allowed to warm to room temperature overnight. The solvent was removed in vacuo and the aqueous layer was extracted with diethyl ether, then acidified to pH 2 by addition of 4M hydrochloric acid. The aqueous layer was extracted with diethyl ether (3x40 ml), and the combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated in vacuo to give the title compound as white crystals (6.02 g, 84%). <BR> <BR> <BR> <BR> <BR> <P>'H NMR (CDCI3): 5/ppm 7.68-7.30 (5H, m), 4.78-4.68 (2H, m), 3.12-3.10 (2H, d, J = 6.9 Hz), 2.76 (1 H, m), 1.91-1.39 (11 H, m), 1.20-1.00 (2H, m).

'3C NMR (CDCI3): b/ppm 180. 1,137.7,129.0,128.9,128.5,78.0,53.9,42.9,38.3, 0,25.5.

LRMS: 276 [M-H], 553 [2M-H].

Example 6 2 (R)-[(N-Formyl-N-hyd roxyamino)-methyl]-hexanoic acid-[2, 2-dimethyl-1 (S)-(1- methyl-1 H-imidazote-2-carbonyt)-propyl]-amide. The title compound was prepared as described in Scheme 2. The experimental details of the synthesis and relevant spectroscopic data are described below.

STEP A: 2 (S)-Amino-N-methoxy-3,3, N-trimethyl-butyramide To a solution of [1 (S)- (methoxy-

methyl-carbamoyl)-2, 2-dimethylpropyl]-carbamic acid-tert-butyl ester (1.686 g, 6.15 mmol) in dichloromethane (20 mL) at 0 °C was added trifluoroacetic acid (17 mL). The reaction was allowed to stand for 16 hours at <5 °C before the solvents were removed in vacuo to give a bright yellow oil. The residue was dissolved in methanol (30 mL) and was treated portionwise with Dowex 1X8-400 basic resin until pH 9. Filtration and removat of the solvents in vacuo gave the title compound as a pale yellow oil (990 mg, 92 %). The material was used without further purification.

.'H NMR (CDC13): b/ppm 3.70 (3H, s), 3.61 (1 H, bs), 3.20 (3H, s), 1.60 (2H, bs), 0.98 (9H, s).

LRMS: (m/z) 175 (M+H) +.

STEP B: 2 (R)- [ (N-Benzyloxyamino)-methyl]-hexanoic acid- [1' (S)- (methoxy-methyl- carbamoyl)-2', 2'-dimethylpropyl] amide To a suspension of 2 (R)- (N-benzyloxyamino-methyl)-hexanoic acid (1.430 g, 5.17 mmol, 1.1 eqv) in DMF (20 mL) at 0 °C was added EDC (1.190 g, 5.64 mmol, 1.2 eqv) and 1-hydroxybenzotriazole (84 mg, 10 mol%). The mixture was allowed to stir at 0 °C for 45 minutes before a solution of 2 (S)-amino-N-methoxy-3,3, N-trimethyl- butyramide (900 mg, 4.7 mmol, 1 eqv) in DMF (5 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvents were removed in vacuo and the residue dissolved in ethyl acetate (75 mL) and 10% w/v aqueous citric acid (50 mL). The aqueous phase was extracted with ethyl acetate (3 x 75 mL) and the combined organic layers washed with saturated sodium hydrogen carbonate solution (100 mL) and brine (2 x 100 mL). The organic phases were dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (SiO2,25% ethyl acetate in hexanes) gave the title compound as a clear oil (1.43 g, 68 %).

'H NMR (CDC13): b/ppm 7.35 (5H, m), 6.73 (1H, bd, J = 10.0 Hz), 5.70 (1H, bs), 5.05 (1 H, d, J = 10.0 Hz), 4.74 (2H, s), 3.78 (3H, s), 3.20 (3H, s), 3.07 (2H, m), 2.50 (1H, m), 1.65 (1 H, m), 1.45 (1 H, m), 1.25 (4H, m), 0.98 (9H, s), 0.86 (3H, t, J = 7.0 Hz).

LRMS: (m/z) 408 (M+H) +.

STEP C: 2 (R)-[(N-Benzyloxyamino)-methyl]-hexanoic acid-[2, 2-dimethyl-1 (S)-(1- methyl-1H-imidazole-2-carbonyl)-propyl]-amide.

To a solution of N-methyl-imidazole (246 mg, 3 mmol, 6 eqv), in dry freshly distilled THF (5 mL) under argon at-78 °C was added dropwise n-BuLi (1.84 mL, 1.6M in . hexanes, 3.0 mmol, 6 eqv) such that an internal temperature of <-70 °C was maintained. The reaction was allowed to stir at-70 °C for 90 minutes after which time a solution of 2 (R)- [ (N-benzyloxyamino)-methyl]-hexanoic acid- [1' (S)-(methoxy- methyl-carbamoyl)-2', 2'-dimethyipropyl] amide (204 mg, 0.5 mmol, 1eqv) in freshly distille THF (2 mL) was added dropwise such that an internal temperature of <-70 °C was maintained. The reaction was allowed to stir at-70 °C for five hours before saturated aqueous ammonium chloride solution (10 mL) was added and the solution allowed to warm to room temperature. The aqueous phase was extracted with ethyl acetate (3 x 50 mL), and the organic phases combined and washed with water (3 x 50 mL) and brine (50 mL). The organic phase was dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil. Purification by column chromatography (SiO2, 30 % hexanes in ethyl acetate) gave the title product as a colourless oil (77 mg, 36 %).

'H NMR (CDCI3): b/ppm 7.33 (5H, m), 7.17 (1H, s), 7.03 (1H, s), 5.75 (1 H, bs), 5.65 (1H, d, J = 9.1 Hz), 4.75 (2H, s), 3.98 (3H, s), 3.10 (2H, m), 2.54 (1H, m), 1.90 (1 H, bm), 1.58 (1 H, m), 1.40 (1 H, m),

1.23 (4H, m), 0.99 (9H, s), 0.80 (3H, t, J = 6.7 Hz).

LRMS: (m/z) 429 (M+H) +.

STEP D: 2 (R)- [ (N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid- [2, 2-dimethyl- 1(S)- (1-methyl-1 H-imidazole-2-carbonyl)-propyl]-amide.

To a solution of 2(R)-[(N-benzyloxyamino)-methyl]-hexanoic acid-[2,2-dimethyl-1 (S)- (1-methyl-1 H-imidazole-2-carbonyl)-propyl]-amide (77 mg, 0.18 mmol) in dichloromethane (2 mL) at 0 °C was added formylacetic anhydride (50 s1L, 0.54 mmol, 3 eqv) and the reaction allowed to stir at room temperature. After 2 hours the solvents were removed in vacuo and the residue azeotroped with toluene (2 x 30 mL). The product was placed under high vacuum for several hours to give the title compound as an off white waxy solid (76 mg, 93 %).

'H NMR (CDCI3): #/ppm 8.30-7.80 (1 H, m), 7.40 (5H, bm), 7.19 (1H, bs), 7.05 (1 H, bs), 5.55 (1 H, bd, J = 9.3 Hz), 5.15-4.70 (2H, bm), 3.96 (3H, bs), 3.80 (1 H, bm), 3.15 (1 H, bm), 2.60 (1 H, m), 1.70-0.70 (18H ; m).

LRMS: (m/z) 456 (M+H) +.

STEP E: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-[2,2-dimethyl- 1(S)- (1-methyl-1 H-imidazole-2-carbonyl)-propyl]-amide.

To a solution of 2 (R)-[(N-benzyloxy-N-formylamino)-methyl]-hexanoic acid-[2, 2- dimethyl-1 (S)- (1-methyl-1 H-imidazole-2-carbonyl)-propyl]-amide. (76 mg, 0.17 mmol) in methanol (2 mL) was added a slurry of 10% Pd/C (10 mg) in ethyl acetate (1 mL).

Hydrogen gas was bubbled through the reaction for 15 minutes after which time the reaction was allowed to stir under one atmosphere of hydrogen for 2 hours. The reaction was flushed with argon and filtered through glass wool. The solvents were removed in vacuo to afford the title compound as a hygroscopic white crystalline solid (43 mg, 70%).

'H NMR (CD30D): 6/ppm 8.26 (0.3H, s), 8.22 (0.7H, d, J = 9.0Hz), 8.10 (0.3H, d, J = 8. OH), 7.84 (0.7H, s), 7.35 (1 H, s), 7.14 (1H, s), 5.71 (1H, m), 3.99 (3H, s), 3.72 (1 H, m), 3.40 (0.5H, dd, J = 14.1,4.6Hz), 3.31 (0.5H, m), 3.05 (0.7H, m), 2.88 (0.3H, m), 1.60-1.10 (6H, m), 0.99 (4H, s), 0.97 (5H, s), 0.82 (3H, t, J = 6.6Hz). '3C NMR (CDC13): b/ppm 4,65.2,56.5,48.2,47. 9.

2,30.4,26.6 and 17.2.

LRMS: (m/z) 365 (M-H)-, 367 (M+H) +.

MIC (E. colza: 25 μM MIC (S. capifis): 200 pM Example 7 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-[2, 2-dimethyl-1 (S)- (pyridine-2-carbonyl)-propyl]-amide The title compound was prepared from 2-bromopyridine as outlined in Scheme 2, in an analogous manner to 2 (R)- [ (N-formyl-N-hydroxyamino)-methyl]-hexanoic acid- [2,2-dimethyl-1 (S)- (1-methyl-1 H-imidazole-2-carbonyl)-propyl]-amide. The relevant spectroscopic data are described below.

STEP C: 2 (R)-[(N-Benzyloxyamino)-methyl]-hexanoic acid-[2,2-dimethyl-1 (S)- (pyridine-2-carbonyl)-propyl]-amide.

Purification by column chromatography (SiO2,30 % to 50 % ethyl acetate in hexanes) gave the title product as a colourless oil (160 mg, 60 %).

'H NMR (CDCl3) : d/ppm 8.72 (1 H, m), 8.05 (1 H, m), 7.82 (1 H, m), 7.45 (1 H, m), 7.40 -7.28 (5H, m), 7.00 (1H, bd, J = 9.3 Hz), 6.22 (1 H, d, J = 9.3 Hz), 5.74 (1 H, bs), 4.76 (2H, s), 3.11 (2H, m), 2.52 (1H, m), 1.58 (1H,,m), 1.40 (1 H, m), 1.22 (4H, m), 0.95 (9H, s), 0.81 (3H, t, J = 6.6 Hz).

LRMS: (m/z) 426 (M+H)'.

STEP D: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-[2, 2-dimethyl- 1(S)- (pyridine-2-carbonyl)-propyl]-amide.

The title compound was isolated as a pale yellow waxy solid (162 mg, 90 %).

'H NMR (CDCI3): #/ppm 8.75 (1 H, m), 8.35-7.80 (4H, m), 7.60-7.10 (5H, m), 6.10 (1H, m), 4.90 (2H, m), 3.75 (2H, bm), 2.90 (2H, bm), 1.60-1.10 (6H, bm), 0.90 (9H, s), 0.85 (3H, m).

LRMS: (m/z) 454 (M+H) +.

STEP E: 2 (R)-[(N-formyl-N-hydroxyamino)-methyl]-hexanoic acid-[2,2-dimethyl- 1(S)- (pyridine-2-carbonyl)-propyl]-amide.

The title compound was isolated as a hygroscopic white crystalline solid (113 mg, 94 %).

'H NMR (CD30D): #/ppm 8.72 (1H, m), 8.27 (0.3H, s), 8.10-7.90 (2H, m), 7.85 (0.7H, s), 7.59 (1 H, m), 7.40-7.20 (1H), 6.18 (1H, m), 3.85-3.58 (1.7H, m), 3.41 (0.3H, dd, J = 14.2,4.7Hz), 3.05 (0.7H, m), 2.89 (0.3H, m), 1.60-1.05 (6H, m), 0.97 (3.5H, s), 0.95 (5.5H, s), 0.79 (3H, t, J = 6.7Hz).

'3C NMR (CD30D): #/ppm 9,122.3, 8.

LRMS: (m/z) 364 (M+H) +.

MIC (E. Coli): 12.5 µM MIC (S. Capitis): 50 uM Example 8 2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(benzofuran-2- carbonyl)-2', 2'-dimethylpropyl) amide.

The title compound was prepared from 2-lithiobenzofuran as outlined in Scheme 2, in an analogous manner to 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- [2', 2'-dimethyl-l' (S)- (l-methyl-1 H-imidazole-2-carbonyl)-propyl]-amide. The relevant spectroscopic data are described below.

STEP C: 2 (R)- [ (N-Benzyloxyamino)-methyl]-hexanoic acid- [1' (S)- (bezofuran-2- carbonyl)-2', 2'-dimethyl-propyl]-amide.

Purification by column chromatography (SiO2,25% ethyl acetate in hexanes) gave the title compound as a colourless oil (43 mg, 19 %).

'H NMR (CDCI3): 7.90-7.20 (10H, m), 7.05 (1H, bd, J = 9.2 Hz), 5.72 (1 H, bs), 5.45 (1H, d, J = 9. 2 Hz), 4.76 (2H, s), 3.11 (2H, m), 2.53 (1H, m), 1.80-1.10 (6H, m), 1.03 (9H, s), 0.82 (3H, m).

LRMS: (m/z) 465 (M+H) +.

STEP D: 2 (R)- [ (N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid- [1' (S)- (bezofuran-2-carbonyl)-2', 2'-dimethyl-propyl]-amide.

Purification by column chromatography (SiO2,2: 1 ethyl acetate: hexanes) gave the title compound as a clear oil (24 mg, 52 %).

'H NMR (MeOD): 8.13 (0.5H, bs), 7.90 (0.5H, bs), 7.81 (2H, m), 7.70-7.25 (8H, m), 5.25 (1 H, m), 4.90 (2H, m), 3.75 (2H, m), 2.90 (1 H, m), 1.60-1.00 (6H, m), 0.98 (9H, s), 0.71 (3H, m).

LRMS: (m/z) 493 (M+H) +, 515 (M+Na) +.

STEP E: 2 (R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- [1 (S)- (bezofuran- 2-carbonyl)-2,2-dimethyl-propyl]-amide.

The title compound was isolated as a hygroscopic white crystalline solid (20 mg, 100%).

'H NMR (MeOD): 8.27 (0.3H, s), 7.85 (1.7H, m), 7.80 (1 H, d, J=7.8Hz), 7.62 (1 H, d, J=8.4Hz), 7.54 (1 H, t, J=7.8Hz), 7.35 (1 H, m), 5.35 (1 H, br. s), 3.78 (1 H, m), 3.62 (0.3H, dd, J=14.0,5.6Hz), 3.42 (0.7H, dd, 7Hz), 3.09 (0.7H, m), 2.91 (0.3H, m), 1.42 (2H, m), 1.25-0.95 (13H, bm), 0.80-0.65 (3H, m).

"C NMR (MeOD): 6,125.7,125.2,116.3, 6,27.7,24.0,14.5.

LRMS: (m/z) 401 (M-H)-, 403 (M+H) +, 425 (M+Na) +.

MIC (E. coll9: 6.25 tM MIC (S. capitis): 1.6 μM Example 9 N- [1 (S)- (Benzofuran-2-carbonyl)-2, 2-dimethylpropyl]-3'-cyclopentyl-2' (R)- [ (N-formyl-<BR> N-hydroxyamino)-methyl]-propionamide The title compound was prepared as described in Scheme 3 and the General Protocol (GP). Experimental details and relevant spectroscopic data are described below. OMe Step A O V 0 HON H 4 Reagents and conditions: Step A: 2-lithiobenzofuran, THF-70 to-400C Scheme 3 0 R2 R1 R1 St H N R1 Step GPB H O Step GPC R2 N R1 N-CHO >-Fi O N-CHU OU R1 = substituted aryl or 2-benzofuranyl R2 = n-Butyl or Cyclopentylmethyl Reagents and conditions: Step GPA: dioxan Step GPB: EDC. HOBT and either oracid in2(R)-[(N-Benzyloxy-N-formylamino)-methyl]-3-cyclopentyl-propionicacid DMF Step GPC: wt%10 General Protocol (GP) STEP A: [1 (S)- (Benzofuran-2-carbonyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester.

A solution of benzofuran (4.24 g, 36 mmol) in dry THF (20 mL) under argon was cooled to-78 °C. n-Butyllithium (22.5 mL, 36 mmol, 1.6M in hexanes) was added dropwise such that an internal temperature below-65 °C was maintained. The reaction was allowed to stir at-78 °C for two hours during which time 2- lithiobenzofuran precipitated as a white solid. The suspension of 2-lithiobenzofuran was added dropwise to a cooled (-78 °C) solution of [1 (S)- (Methoxy-methyl-carbamoyl)-2,2-dimethylpropyl]-carbamic acid-tert-butyl ester (3.34 g, 12 mmol) in THF (30 mL) via cannula such that an internal temperature of below-65 °C was maintained. The yellow solution was allowed to stir at-70 °C for 30 minutes and-40 °C for a further 3 hours. The reaction was quenched by addition of saturated ammonium chloride solution (200 mL). The aqueous phase was extracted with ethyl acetate (3 x 150 mL) and the combined organic extracts washed with brine (2 x 200 mL), dried over magnesium sulphate, filtered and the solvents removed in vacuo to give a crude yellow oil. Purification by column chromatography (SiO2,10 % ethyl acetate in hexanes) gave the title compound as a yellow solid (3.45 g, 87 %).

'H NMR (CDC13): 5/ppm 7.70 (2H, m), 7.62 (1 H, m), 7.50 (1 H, m), 7.31 (1H, m), 5.41 (1H, bd, J =

9.1 Hz), 5.07 (1H, bd, J = 9.7 Hz), 1.43 (9H, s), 1.02 (9H, s).

LRMS: (m/z) 354 (M+Na).

STEP GPA: 2 (S)-Amino-1-benzofuran-2-yl-3,3-dimethylbutan-1-one.

[1 (S)- (Benzofuran-2-carbonyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester (700 mg, 2.11 mmol) was dissolved in 1,4-dioxan saturated with HCI (10 mL) and the yellow solution allowed to stir at room temperature for 18 hours.

The reaction was added to saturated sodium bicarbonate solution (50 mL) (CAUTION!) and the pH adjusted to 10 with the addition of 1 M sodium carbonate.

The aqueous mixture was extracted with ethyl acetate (3 x 100mL) and the combined organic extracts washed with brine (3 x 100 mL), dried over magnesium sulphate, filtered and the solvents removed in vacuo to give the title compound as a pale yellow solid (480 mg, 98 %).

Alternatively the a-aminoketones were isolated as hydrochloride salts by removal of the HCI/1, 4-dioxan in vacuo.

'H NMR (CDCI3): â/ppm 7.72 (1 H, d, J = 7.8 Hz), 7.55 (2H, m), 7.48 (1 H, m), 7.32 (1H, t, J = 7.5 Hz), 4.12 (1H, s), 1.65 (2H, bs), 1.02 (9H, s).

STEP GPB: N- [1 (S)- (Benzofuran-2-carbonyl)-2, 2-dimethylpropyl]-3'-cyclopentyl- 2'(R)-[(N-benzyloxy-N-formylamino)-methyl]-propionamide.

To a solution of 2 (R)- [ (N-Benzyloxy-N-formylamino)-methyl]-3-cyclopentyl-propionic acid (247 mg, 0.81 mmol) in DMF (5 mL) at 0 °C was added EDC (157 mg, 0.81 mmol) and HOBT (22 mg, 20 mol %) and the mixture allowed to stir at 0 °C for 45 minutes. A solution of 2 (S)-Amino-1-benzofuran-2-yl-3, 3-dimethylbutan-1-one (149 mg, 0.65 mmol) in DMF (2 mL) was added and the reaction allowed to stir at ambient temperature for 18 hours. The solvent was removed in vacuo and the residue dissolved in ethyl acetate (50 mL) and ammonium chloride solution (50 mL).

The organic layer was separated and the aqueous phase extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were dried over magnesium sulphate, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (SiO2,2: 1 hexanes: ethyl acetate) gave the title compound as a clear oil (196 mg, 58 %).

Alternatively where the hydrochloride salts of the a-aminoketones were used the free amine was generated by the addition of 2 equivalents of TEA to the DMF solution of the a-aminoketone prior to addition to the HOBT ester.

'H NMR (MeOD): b/ppm 8.42-8.25 (1 H, bm), 8.13 (0.5H, m), 7.90 (0.5H, m), 7.78 (1 H, s), 7.60 (1 H, m), 7.59-7.30 (7H, m), 5.25 (1 H, m), 4.90 (2H, m), 3.72 (1.5H, m), 3.33 (0.5H, m), 2.95 (1 H, m), 1.75 (1 H, m), 1.65-1.10 (8H, m), 0.98 (9H, s), 0.94 (2H, m).

LRMS: (m/z) 541 (M+Na) + STEP GPC: N- [1 (S)- (Benzofuran-2-carbonyl)-2, 2-dimethylpropyl]-3'-cyclopentyl- 2'(R)-[(N-formyl-N-hydroxyamino)-methyl]-propionamide.

N- [1 (S)- (Benzofuran-2-carbonyl)-2, 2-dimethyipropyl]-3'-cyclopentyl-2' (R)- [ (N- benzyloxy-N-formylamino)-methyl]-propionamide (197 mg, 0.38 mmol) was dissolved in methanol (15 mL) under argon and a slurry of palladium on charcoal (20 mg) in ethyl acetate (1 mL) was added and hydrogen bubbled through the reaction for 10 minutes. An atmosphere of 1 bar of hydrogen was maintained via balloon and the reaction allowed to stir at ambient temperature for 1 hour. The reaction was filtered through glass wool and the solvents removed in vacuo. The residue was purified by reverse phase preparative HPLC to give the title compound as a white crystalline solid (84 mg, 52 %).

'H NMR (MeOD): 6/ppm 8.28 (0.4H, s), 7.83 (2.6H, m), 7.65-7.45 (2H, m), 7.35 (1 H, t, J=7. 0Hz), 5.36 (1H, m), 3.77 (1 H, dd, J=14.1,9.5Hz), 3.61 (0.3H, dd, J=14.0, 5.4Hz), 3.43 (0.7H, dd, J=14.0,4.6Hz), 3.10 (0.7H, m), 2.93 (0.3H, m), 1.82-1.15 (9H, m), 1.05 (9H, s), 1.10-0.80 (2H, m).

13C NMR (MeOD): #/ppm 8,154.3,130.4,129.6,125.7,125.2,
5,45.4,39.4,38.1,36.3,34.4,33.8,27.7,26.3,26.2.

LRMS: (m/z) 451 (M+Na) +.

MIC (E. coli): 6.25 M MIC (S. capitis): 0.7 µM Example 10 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid pentafluorophenyl ester The title compound was prepared as described in Scheme 4. The experimental details of the synthesis and relevant spectroscopic data are described below. F F F OH Step A p Ste- B O \ F F N-O N-O ß \ OH I \ OH I \ Reagents and conditions: Step A: Formyl acetic anhydride, TEA, THF, 0 °C, 1 hour then RT, 1 hour; Step B: Pentafluorophenol, EDC, EtOAc, 0 °C to RT, O/N.

Scheme 4 Step A: 2 (R)- (N-Benzyloxy-N-formylamino)-methyl)-hexanoic acid To a solution of 2 (R)-(N-benzyloxyamino-methyl)-hexanoic acid (30.6 g, 0.12 mol) in dry THF (300 ml) was added formic acetic anhydride (26.8 ml, 0.31 mol) at 0 °C.

Triethylamine (18.5 ml, 0.13 mol) was added and the reaction mixture was stirred for 1 hour at 0 °C and 60 hours at room temperature. The solvent was removed in vacuo to yield the title compound as a yellow oil (33.6 g, 99%) which was used in Step B without further purification.

'H NMR (CDCI3): 6/ppm (rotamers) 8.14 (0.7H, br s), 8.00 (0.3H, br s), 7.50-7.25 (5H, m), 5.07-4.70 (2H, m), 3.95-3.52 (2H, m), 2.78 (1 H, br s), 1.72-1.20 (6H, m) and 0.89 (3H, br s).

LRMS: (m/z) 280 (M+H)" Step B: 2 (R)- [ (N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid pentafluorophenyl ester To a solution of 2 (R)- (benzyloxy-formylamino)-methyl)-hexanoic acid (33.6 g, 0.12 mol) in dry THF (500 ml) was added pentafluorophenol (44.3 g, 0.24 mol), EDC (27.7 g, 0.14 mol) and hydroxybenzotriazole (16.2 g, 0.12 mol). The reaction was stirred overnight at room temperature. The solvent was removed in vacuo and the residue was dissolved in ethyl acetate, washed with 1 M Na2CO3 (3 x 500 ml) and water (1 x 500 ml) and dried over MgSO4 and concentrated in vacuo to yield a yellow oil (60 g). The product was purified by flash chromatography (SiO2,5: 1, hex: EtOAc to 1: 2 hex: EtOAc) to yield a clear oil (42.0 g, 79%).

'H NMR (CDCI3): 6/ppm (rotamers) 8.15 (0.7H, br s), 8.01 (0.3H, br s), 7.60-7.21 (5H, m), 5.00-4.70 (2H, m), 4.04-3.72 (2H, m), 3.09 (1 H, br s), 1.85-1.57 (2H, m), 1.50-1.26 (4H, m), 1.00-0.82 (3H, m).

LRMS: (m/z) 468 (M+Na), 446 (M+H) +.

Example 11 2 (R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid [1'- (2,4-dimethoxy- benzoyl)-

2', 2'-dimethyl propyl]-amide The title compound was prepared as described in Scheme 5. The experimental details of the synthesis and relevant spectroscopic data are described below. 0 F OMe OMe Y H 0 0 0 N FF H O OMe F 0 OMe Step C 0-4 rY'SteoD 0-4 rY !!!'StepD t! t H!!! if H l! l! OMe OMe Step D N H 0 OMe H 0 OMe N-CHO 0 OMe N-CHO OH OBn Reagents and conditions: Step A: 4-lithio-3-methoxyanisole, THF-700C Step B: dioxan Step C: pentafluorophenylester,acid TEA and DCM.

Step D:H2/Pd/C STEP A: [1 (S)- (2, 4-Dimethoxy-benzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester.

To a solution of 1-bromo-2,4-dimethoxybenzene (482 mg, 2.22 mmol) in dry THF (10 mL) at-78 °C under argon was added dropwise t-BuLi (2.96 mL, 4.44 mmol, 1.5M in pentanes). After addition was complete the reaction mixture was allowed to stir at -75 °C for one hour. Meanwhile a solution of 2-tert-Butoxycarbonylamino-3,3- dimethyl-butyric acid pentafluorophenyl ester (Example 14) (400 mg, 1.01 mmol) in dry THF (5 mL) was prepared at-75 °C under argon. The solution of 4-lithio-3-methoxyanisole was then added dropwise via cannula such that an internal -temperature of less than-70 ° C was maintained. The reaction was allowed to stir at -70 °C for 4 and a half hours before saturated ammonium chloride solution (30 mL) was added. The aqueous phase was extracted with ethyl acetate (3 x 30 mL) and the combined organic extracts washed with 1 M sodium carbonate solution (3 x 100 mL) and brine (2 x 100 mL). The ethyl acetate phase was dried over magnesium sulphate, filtered and the solvents removed in vacuo to give a clear oil. Purification by column chromatography (SiO2,6: 1 hexanes: ethyl acetate) gave the title compound as a clear oil (239 mg, 68 %).

'H NMR (CDCI3): S/ppm 7.70 (1 H, d, J = 8.6 Hz), 6.52 (1 H, dd, J = 8.7,2.2 Hz), 6.42 (1 H, m), 5.50 (1 H, m), 5.40 (1 H, d, J = 9.7 Hz), 3.91 (3H, s), 3.86 (3H, s), 1.45 (9H, s), 0.88 (9H, s).

LRMS: (m/z) 374 (M+Na) + STEP B: 2 (S)-Amino-1- (2, 4-dimethoxy-phenyl)-3, 3-dimethyl-butan-1-one. HCI To [1 (S)- (2, 4-Dimethoxy-benzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester (239 mg) at 0 °C was added 1-4 dioxan saturated with HCI (3 mL). The reaction solution was allowed to stir for 18 hours before the solvents were removed in vacuo and the residue azeotroped with DCM (3 x 10 mL) to give the title compound as a yellow solid (224 mg).

'H NMR (MeOD): ã/ppm 7.74 (1 H, d, J = 9.3 Hz), 6.89 (2H, m), 5.12 (1H, s), 3.97 (3H, s), 3.89 (3H, s), 0.99 (9H, s).

LRMS: (m/z) 252 (M+H) + STEP C: 2 (R)-[(N-Benzyloxy-N-formylamino) methyl]-hexanoic acid [1'(S)-(2,4- dimethoxy-benzoyl)-2', 2'-dimethylpropyl]-amide To a solution of 2-{2-[(N-Benzyioxy-N-formylamino)-methyl]-hexanoylamino}-3,3- dimethyl-butyric acid pentafluorophenyl ester (303 mg, 0.681 mmol) in DCM (3 mL) -at 0 °C was added triethylamine (131 mg, 1.29 mmol) followed by a solution of 2 (S)- Amino-1- (2, 4-dimethoxy-phenyl)-3, 3-dimethyl-butan-1-one. HCI in DCM (2 mL). The reaction was allowed to warm to ambient temperature and stirred for 18 hours.

Saturated ammonium chloride solution (50 mL) was added and the aqueous phase extracted with ethyl acetate (3 x 30 mL). The organic phases were washed with water (100 mL), 1 M sodium carbonate solution (3 x 100 mL) and brine (100 mL), dried over magnesium sulphate, filtered and the solvents removed in vacuo to give a crude brown oil. Purification by column chromatography (SiO2,1: 1 hexanes: ethyl acetate) gave the title product as a clear oil (153 mg 44 %).

'H NMR (CDCl3) : ã/ppm 8.13 (0.5, bs), 7.91 (0.5, bs), 7.69 (1 H, bd, J = 8.5 Hz), 7.60 -7.30 (5H, m), 6.54 (1 H, dd, J = 8.7,2.3 Hz), 6.40 (2H, m), 5.72 (1 H, m), 5.00 and 4.80 (2H, m), 3.90 (3H, s), 3.85 (3H, s), 3.70 (1H, m), 3.10 (1H, m), 2.58 (1H, m), 1.55-1.10 (6H, m), 1.00-0.76 (12H, m).

LRMS: (m/z) 513 (M+H) +, 535 (M+Na) +.

STEP D: 2 (R)-[(N-Formyl-N-hydroxyamino)methyl]-hexanoic acid [1' (S)- (2,4- dimethoxy-benzoyl)-2', 2'-dimethylpropyl]-amide 2 (R)-[(N-Benzyloxy-N-formylamino)methyl]-hexanoic acid [1' (S)- (2,4-dimethoxy- benzoyl)-2', 2'-dimethylpropyl]-amide (154 mg, 0.30 mmol) was dissolved in methanol (10 mL) under argon and a slurry of palladium on charcoal (15 mg) in ethyl acetate (1 mL) was added and hydrogen gas bubbled through the reaction solution for 10 minutes. The reaction was allowed to stir under a hydrogen atmosphere (ballon) for one hour. The reaction was filtered through glass wool and the solvents removed in vacuo to give the title compound as a white crystalline solid (99 mg, 78 %).

'H NMR (MeOD): â/ppm 8.27 (0.4H, s), 8.19 (0.6H, bd, J=9. OHz), 8.10 (0.4H, bd, J=9. OHz), 7.85 (0.6H, s), 7.63 (1 H, m), 6.62 (2H, m), 5.72 (1 H, m), 3.90 (3H, s), 3.86 (3H, s), 3.85 (1 H, m), 3.61 (0.4H, m), 3.41 (0.6H, dd, J=14.2,4.6Hz), 3.05 (0.6H, m), 2.90 (0.4H, m), 1.70-1.10 (6H, m), 0.90 (9H, bs), 0.82 (3H, m).

13C NMR (MeOD): 5/ppm 9, 2,31.6,30.6,27.9,24.0,14.6.

LRMS: (m/z) 421 (M-H)-, 423 (M+H) + 445 (M+Na) +.

MIC (E. colt): 25 uM MIC (S. capitis): 25 s1M Example 12 2 (R)-[(N-Formyl-N-hyd roxyamino)-methyl]-hexanoic acid [1' (S)- (4-hydroxy-benzoyl)- 2',2'-dimethylpropyl]-amide The title compound was prepared as described in Scheme 6. The experimental details of the synthesis and relevant spectroscopic data are described below. OH OMe OH p/ Step A I St p B O-_N HZN H I riz OBI OBn Step C OH H N-CHO Reagents and conditions: OH Step A: Boron tribromide Step B: EDC, HOBT and 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl] hexanoic acid, DMF Step C : H2/Pd/C 10 wt% Scheme 6 STEP A: 2 (S)-Amino-1- (4-hydroxy-phenyl)-3,3-dimethyl-butan-1-one To a solution of (1 (S)- (4-Methoxybenzoyl) I-2, 2-dimethylpropyl) carbamic acid-tert- butyl ester (191 mg, 0.86 mmol) in 1,2-dichloroethane (15 mL) at 0 °C was added dropwise BBr3 (3 mL, 3 mmol, 1.0 M in DCM). The brown solution was allowed to warm to room temperature and stirred for 18 hours. The reaction mixture was again cooled to 0 °C and 1 M HCI in methanol (15 mL) added cautiously. The yellow solution was allowed to warm to ambient temperature and stirred for two hours before the solvents were removed in vacuo to give a yellow solid. The residue was dissolved in 1 M HCI (30 mL) and washed with toluene (15 mL) and diethyl ether (15 . mL). The pH of the aqueous phase was adjusted to 8 with the addition of solid sodium bicarbonate. The aqueous phase was then extracted with ethyl acetate (3 x 70 mL), dried over magnesium sulphate and filtered. The solvents were removed in vacuo to give the title compound as a pinkish solid (148 mg, 83 %).

'H NMR (MeOD): 5/ppm 7.88 (2H, d, J = 8.8 Hz), 6.83 (2H, d, J = 8.9 Hz), 4.32 (1 H, s), 0.93 (9H, s).

LRMS: (m/z) 206 (M-H)-, 208 (M+H) + STEP B: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid [1' (S)- (4- hydroxy-benzoyl)-2, 2-dimethylpropyl]-amide To a solution of 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid (229 mg, 0.82 mmol) in DMF (10 mL) at 0 °C was added EDC (159 mg, 0.82 mmol) and HOBT (26 mg, 20 mol %) and the mixture allowed to stir at 0 °C for 30 minutes. A solution of 2 (S)-Amino-1- (4-hydroxy-phenyl)-3, 3-dimethyl-butan-1-one (140 mg, 0.68 mmol) in DMF (5 mL) was added and the reaction allowed to stir at ambient temperature for 18 hours. The solvent was removed in vacuo and the residue dissolved in ethyl acetate (30 mL) and water (70 mL). The organic layer was separated and the aqueous phase extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were dried over magnesium sulphate, filtered and the solvents removed in vacuo to give a crude off white foam. Purification by column chromatography (SiO2, 1: 1 hexanes: ethyl acetate) gave the title compound as a white sticky foam (151 mg, 47 %).

'H NMR (CDCI3): ã/ppm 8.93 (1H, bs), 8.15 (0.5H, bs), 7.95 (0.5H, bs), 7.84 (2H, d, J = 8.8 Hz), 7.38 (5H, m), 6.88 (2H, d, J = 8.7 Hz), 6.48 (1H, bd, J = 9.1 Hz), 5.43 (1 H, m), 4.90 (2H, bm), 3.75 (1.5H, bm), 3.12 (0.5H, bm), 2.60 (1H, m), 1.70-1.05 (6H, m), 0.93 (9H, s).

LRMS: (m/z) 491 (M+Na)' . STEP C: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid [1' (S)- (4-hydroxy- benzoyl)-2', 2'-dimethylpropyl]-amide 2 (R)-[(N-Benzyloxy-N-formylamino) methyl]-hexanoic acid [1' (S)- (4-hydroxy-benzoyl)- 2', 2'-dimethytpropyl]-amide (151 mg, 0.32 mmol) was dissolved in methanol (15 mL) under argon and a slurry of palladium on charcoal (20 mg) in ethyl acetate (1 mL) was added and hydrogen gas bubbled through the reaction solution for 10 minutes.

The reaction was allowed to stir under a hydrogen atmosphere (ballon) for one hour. The reaction was filtered through glass wool and the solvents removed in vacuo to give the title compound as a white crystalline solid (119 mg, 98 %).

Purification on the ASPEC preparative HPLC system gave the title product in >95 % purity (98 mg, 81 %).

'H NMR (MeOD): ã/ppm 8.27 (0.3H, s), 8.23 (0.7H, bd, J=9.4Hz), 8.11 (0.3H, bd, J=9.2Hz), 7.92 (2H, d, J=8.8Hz), 7.86 (0.7H, s), 6.85 (2H, d, J=8.8Hz), 5.48 (1H, m), 3.80 (1H, m), 3.61 (0.3H, dd, 7Hz), 3.41 (0.7H, dd, J=14.2,4.6Hz), 3.02 (0.7H, m), 2.87 (0.3H, m), 1.60-1.30 (2H, m), 1.30-1.10 (4H, m), 0.96 (9H, s), 0.75 (3H, t, J=7. 0Hz).

13C NMR (MeOD): 6/ppm 9, 45.8,45.5,36.3,31.6,30.6,27.9,24.0,14.5.

LRMS: (m/z) 377 (M-H)-, 401 (M+Na) +.

MIC (E. coll): 6.25 µM MIC (S. capitis): 12 µM Example 13 2(R)- [ (N-Benzyloxy-N-formylamino)-methyl]-3-cyclopentyl-propionic acid The title compound was prepared as described in Scheme 7. The experimental details of the synthesis and relevant spectroscopic data are described below. 00 H O H O , OH Step A OH I N-0--\\ N-0 H \--. J')- u°"u H Reagents and conditions: Step A: Formyl acetic anhydride, TEA, THF, 0 °C, 1 hour then RT, 1 hour; Step A: 2 (R)-[(N-BenzylOxy-N-formylamino)-methyl]-3-cyciopentyl-propionic acid 2 (R)- (Benzytoxyamino-methyl)-3-cyclopentyl-propionic acid was prepared as described above.

Formic acetic anhydride (27.78 g, 0.32 mol) followed by TEA (52.7 mL, 0.38mol) were added to a cooled (0 °C) solution of 2 (R)- (benzyloxyamino-methyl)-3- cyclopentyl-propionic acid in THF (180 mL). The reaction mixture was stirred for 1 hour at 0 °C and then at room temperature for 1 hour before the solvent was removed in vacuo. The residue was purified by column chromatography (SiO2,25-100% EtOAc in hexanes) to give the title compound as a colourtess oil (36.10 g, -94%).

'H NMR (CDCI3): #/ppm 10.50-10.15 (1H, m), 8.23-7.87 (1H, m), 7.50-7.10 (5H, m), 5.13-4.67 (2H, m), 3.97-3.54 (2H, m), 2.95-2.67 (1H, m), 2.13-0.93 (11H, m).

LRMS: (m/z) 328 (M + Na)' ; 304 (M-H)-.

Example 14 2 (S)-tert-Butoxycarbonylamino-3,3-dimethyl-butyric acid pentafluorophenyl ester The title compound was prepared as described in Scheme 8. The experimental details of the synthesis and relevant spectroscopic data are described below. F OH Step A BocN H-BocN H I F BocNHF F Reagents and conditions: A. Pentafluorophenol, NMM, EDC, EtOAc, 0 °C to RT, O/N.

Scheme 8 Step A: 2 (S)-tert-Butoxycarbonylamino-3, 3-dimethyl-butyric acid pentafluorophenyl ester 2 (S)-tert-Butoxycarbonylamino-3, 3-dimethyl-butyric acid was prepared from L-tert- leucine according to Step A of Scheme 1.

Pentafluorophenol (8.75 g, 47.5 mmol) dissolved in EtOAc (5 mL) was added to a solution of 2 (S)-tert-butoxycarbonylamino-3, 3-dimethyl-butyric acid (10 g, 43 mmol) in EtOAC (35 mL) and the mixture cooled to 0 °C. NMM (4.75 mL, 43 mmol) followed by EDC (9.12 g, 47.6 mmol) were added to this cooled solution and the reaction mixture was then allowed to warm to room temperature and stirred overnight. The reaction mixture was then diluted with EtOAc (200 mL) and washed with 1 M HCI (2 x 200 mL), 1 M Na2CO3 (3 x 200 mL) and brine, dried over MgSO4 and concentrated in vacuo. The residue was purified by column chromatography (Si02,10% EtOAc in hexanes) to give the title compound as a white solid (12.03 g, 70%).

'H NMR (CDCI3): b/ppm 5.16-4.99 (1H, m), 4.41 (1H, d, J = 9.4), 1.47 (9H, s) and 1.11 (9H, s).

LRMS: (m/z) 420 (M + Na) +.

Example 15 2(R)-[(N-Formyl-N-hyd roxyamino)-methyl]-hexanoic acid-(1'(S)-teff-butyl-2'-oxo-3'-pyridin-2-yl-propyl) amide The title compound was prepared as described in Scheme 9. The experimental details of the synthesis and relevant spectroscopic data are described below.

Scheme 9 N Step A BocNH 0 N Step B (HC') 2H2N OH I N W ° W OH W]UN Step C N N N Step D N \ H II I/ \ H / N-OH N-OBn OAH O ; H Reagents and conditions: Step A. (i) n-BuLi, THF,-40 °C, 1 hour (ii)-78 °C, 2 (S)-tert-butoxycarbonylamino- 3,3-dimethyl-butyric acid pentafluorophenyl ester/THF; Step B. HCI/Dioxane, 2 hours, RT; Step C. (i) 2 (R)-[(benzyloxy-formyl-amino)-methyl]-hexanoic acid, EDC, HOBt, DMF, RT, 1.5 hours (ii) 3 (S)-amino-4,4-dimethyl-1-pyridin-2-yl-pentan-2-one hydrochloride, NMM, DMF, RT, over W/E; Step D. H2, Pd/C, MeOH.

STEP A: (1 (S)-tert-Butyl-2-oxo-3-pyridin-2-yl-propyl)-carbamic acid tert-butyl ester The reaction was carried out under argon in flame dried apparatus. n-BuLi (1.6 M in hexanes, 11.3 mL, 18.1 mmol) was added dropwise to a cooled (-40 °C) solution of 2-picoline (1.64 mL, 16.6 mmol) in THF (30 mL). When addition was complete the solution was stirred at-40 °C for 1 hour before cooling to-78 °C. A solution of 2 (S)- tert-butoxycarbonylamino-3,3-dimethyl-butyric acid pentafluorophenyl ester (3.00 g, 7.6 mmol) in THF (30 mL) was added via a canula, maintaining the reaction temperature below-65 °C. After stirring for 1 hour at-78 °C saturated NH4CI solution (10 mL) was added and the reaction mixture was allowed to warm to room temperature before it was partitioned between EtOAc (200 mL) and saturated NH4CI solution (200 mL). The organic extract was washed with water (200 mL) and brine (200 mL), dried over MgSO4 and concentrated in vacuo. The residue was purified by column chromatography (SiO2,25% Et2O in hexanes) to give the title product as a bright yellow solid (1.01 g, 44%).

'H NMR (CDCI3): B/ppm 8.57-8.51 (0.5H, m), 8.10 (0.5H, d, J = 5.2 Hz), 7.69-7.49 (1H, m), 7.25-7.13 (1H, m), 6.95-6.84 (1 H, m), 5.40-5.28 (1H, m), 5.28-5.14 (0.5H, m), 4.29 (0.5H, d, J = 9.25 Hz), 4.09 (1 H, s), 3.95 (0.5H, d, J = 9.8 Hz), 1.44 (4.5H, s), 1.42 (4.5H, s), 1.02 (4.5H, s) and 1.01 (4.5H, s).

['H NMR is complex due to the presence of E and Z enol tautomers.] LRMS: (m/z) 329 (M + Na) +.

STEP B: (E)-or (Z)-3 (S)-Amino-4,4-dimethyl-1-pyridin-2-yl-pent-1-en-2-ol hydrochloride (1 (S)-tert-Butyl-2-oxo-3-pyridin-2-yl-propyl)-carbamic acid tert-butyl ester (300 mg, 1.0 mmol), was dissolved in dioxane saturated with HCI (20 mL) and the reaction mixture stirred at room temperature for 2 hours.

The mixture was then concentrated in vacuo to give the title compound as a yellow solid (0.37 g) which was used in Step C without further purification.

'H NMR (CD30D): a/ppm 8.91 (1 H, d, J = 5.7 Hz), 8.73-8.60 (1 H, m), 8.20-8.04 (2H, m), 5.16-4.77 (1H, m), 4.45 (1 H, s), 1.23 (9H, s).

STEP C: 2 (R)- [ (N-Benzyioxy-N-formylamino)-methyl]-hexanoic acid (1' (S)-tert-butyl- 2'-oxo-3'-pyridin-2-yl-propyl) amide EDC (0.16 g, 0.83 mmol) followed by HOBt (0.11 g, 0.81 mmoi) was added to a solution of 2 (R)- (benzyloxy-formylamino)-methyl-hexanoic acid (0.18 g, 0.64 mmol) in DMF (3 mL) and the reaction mixture stirred for 1.5 hours at room temperature. A mixture of (E)-or (Z)-3 (S)-amino-4,4-dimethyl-1-pyridin-2-yl-pent-1-en-2-ol hydrochloride (1.0 mmol) and NMM (0.23 mL, 2.1 mmol) in DMF (1.5 mL) was heated until a solution was obtained and added to the reaction mixture which was then stirred at room temperature for 72 hours. The solvent was removed by concentration in vacuo and the residue partitioned between ethyl acetate (30 mL) and water (15 mL). The organic phase was washed with saturated sodium bicarbonate solution (15 mL) and brine (15 mL), dried over MgS04, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO2, 50% ethyl acetate in hexanes) to give the title compound as a bright yellow solid (0.20 g, 68%).

'H NMR (CDCl3) : o/ppm 8.58-6.21 (11 H, m), 5.41-3.55 (6.5H, m), 2.66-2.46 (1 H, m) and 1.73-0.67 (18H, m).

['H NMR is complex due to the presence of E and Z enol tautomers.] LRMS: (m/z) 468 (M + H) +; 466 (M-H)-.

STEP D: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-teff-butyl-2'- oxo-3'-pyridin-2-yl-propyl) amide To a solution of 2 (R)-[(N-benzyloxy-N-formylamino)-methyl]-hexanoic acid (1' (S)-tert- butyl-2'-oxo-3'-pyridin-2-yl-propyl) amide (0.20 g, 0.44mmol) in methanol (40 mL) under an argon atmosphere was added a slurry of 10% Pd/C (20 mg) in ethyl acetate (1 mL). Hydrogen gas was bubbled through the reaction mixture for 5 minutes before leaving the reaction to stir under 1 atmosphere of hydrogen for 10 hours. The reaction mixture was then flushed with argon and filtered through a pad of glass microfibre filters. The filtrate was concentrated in vacuo to give the title compound as a bright yellow glass (0.15 g, 92%).

'H NMR (CDCI3): 5/ppm 8.73-6.65 (6H, m), 5.40-3.94 (2.5H, m), 3.94-3.24 (2H, m), 2.97-2.53 (1H, m), 1.73-1.10 (6H, m), [1.02,1.00,0.98 (9H, 3 x s)] and 0.89-0.63 (3H, m).

['H NMR is complex due to the presence of E and Z enol tautomers.] LRMS: (m/z) 378 (M + H) +; 376 (M-H)-.

MIC (S. capitis): 100 μM Example 16 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid [1' (S)- (4-methanesulfonyl- benzoyl)-2', 2'-dimethyl-propyl] amide The title compound was prepared as described in Scheme 10. The experimental details of the synthesis and relevant spectroscopic data are described below. /F/SOZMe/SOzMe Step A Step B BocNH > BocNH) < (HCI) H N\W502Me 00 0 Step C 0 S02Me S02Me Step D N N N N N O O N-OH N-OBn 0) sH OAH Reagents and conditions: Step A: MeSO2Na, DMSO, 130 °C, O/N ; Step B: HCI/Dioxane, O/N, RT; Step C: (i) 2 (R)-[(Benzyloxy-formylamino)-methyl]-hexanoic acid, EDC, HOBt, DMF, RT, 1.5 hours (ii) 2 (R)- and 2 (S)-amino-1-(4-methanesulfonyl-phenyl)-3,3- dimethyl-butan-1-one hydrochloride, NMM, DMF, RT, O/N; Step D: (i) H2, Pd/C, MeOH, 3.5 hours, (ii) Prep. HPLC.

Scheme 10 STEP A: Racemic mixture of 1 (R)-and 1 (S)- (4-Methanesulfonyl-benzoyl)-2,2- dimethyl-

propyl-carbamic acid-tert-butyl ester 1 (S)- (4-fluorobenzoyi)-2, 2-dimethylpropyl) carbamic acid-tert-butyl ester was prepared as described in steps A to C in Scheme 1 (version 2).

Sodium methane sulphinate (132 mg, 1.3 mmol) was added to a solution of 1 (S)- (4- fluorobenzoyl)-2, 2-dimethylpropyl) carbamic acid-tert-butyl ester (200 mg, 0.6 mmol) in DMSO (4 mL) and the mixture stirred under argon at 130 °C for 17 hours. After cooling to room temperature the reaction mixture was partitioned between diethyl ether (100 mL) and water (100 mL), the organic extract washed with water (100 mL) and brine (100 mL), dried over MgS04, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO2,10% ethyl acetate in hexanes) to give the title compound as a white solid (0.22 g, 73%).

'H NMR (CDCLJ: 8/ppm 8.18 (2H, d, J = 8.4), 8.11-8.01 (2H, m), 5.42-5.27 (1 H, m), 5.13 (1H, d, J = 9.6), 3.08 (3H, s), 1.43 (9H, s) and 0.94 (9H, s).

LRMS: (m/z) 392 (M + Na) +.

STEP B: 2 (R)- and 2 (S)-Amino-1- (4-methanesulfonyl-phenyl)-3, 3-dimethyl-butan-1- one hydrochloride 1 (R)-and 1 (S)- (4-Methanesulfonyl-benzoyl)-2, 2-dimethyl-propyl-carbamic acid-tert-butyl ester (0.22 g, 0.6 mmol), was dissolved in dioxane saturated with HCI (20 mL) and the reaction mixture stirred at room temperature for 17 hours. The mixture was then concentrated in vacuo to give the title compound as a yellow solid which was used in Step C without further purification.

'H NMR (MeOD): 6/ppm 8.34-8.12 (4H, m), 5.12 (1H, s), 3.20 (3H, s) and 1.04 (9H, s).

STEP C: (2R, 1'R)-and (2R, 1'S)-2-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid [1'- (4-methanesulfonyl-benzoyl)-2', 2'-dimethylpropyl] amide . EDC (98 mg, 0.51 mmol) followed by HOBt (70 mg, 0.52 mmol) were added to a solution of 2 (R)-[(benzyloxy-formylamino)-methyl]-hexanoic acid (0.11 g, 0.39 mmol) in DMF (2 mL) and the reaction mixture stirred for an hour at room temperature.

2 (R)- and 2 (S)-amino-1- (4-methanesulfonyl-phenyl)-3, 3-dimethyl-butan-1-one hydrochloride (0.6 mmol) and NMM (0.13 mL, 1.2 mmol) in DMF (1.0 mL) were heated until a solution was obtained, added to the reaction mixture and stirred overnight. The solvent was removed by concentration in vacuo and the residue partitioned between ethyl acetate (40 mL) and 1 M HCI (40 mL). The organic phase was washed with saturated sodium bicarbonate solution (40 mL) and brine (40 mL), dried over MgSO4, filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO2,1.5% methanol in DCM) to give the title compound as a white solid (140 mg, 67%).

'H NMR (CDCI3): 5/ppm 8.30-7.92 (5H, m), 7.51-7.10 (5H, m), 6.50-6.17 (1H, m), 5.66-5.49 (0.4H, m), 5.49-5.33 (0.6H, m), 5.10-4.45 (2H, m), 3.93-3.53 (2H, m), 3.21-2.97 (3H, m), 2.68-2.49 (1H, m), 1.61-1.03 (6H, m) and 1.04-0.73 (12H, m).

LRMS: (m/z) 553 (M + Na) +, 531 (M + H) +.

STEP D: (2R, 1'R)- and (2R, 1'S)-2-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid [1'- (4-methanesulfonyl-benzoyl)-2', 2'-dimethyl-propyl] amide To a solution of (2R, 1'R)-and (2R, 1'S)-2-[(N-Benzyloxy-N-formylamino)-methyl]- hexanoic acid [1'- (4-methanesulfonyl-benzoyl)-2', 2'-dimethylpropyl] amide (140 mg, 0.26 mmoi) in methanol (30 mL) under an argon atmosphere was added a slurry of 10% Pd/C (14 mg) in ethyl acetate (1 mL). Hydrogen gas was bubbled through the reaction mixture for 5 minutes before leaving the reaction to stir under 1 atmosphere of hydrogen for 3.5 hours. The reaction mixture was then flushed with argon and filtered through a pad of glass microfibre

filters. The filtrate was concentrated in vacuo and the residue purified by reverse phase HPLC to give the (2R, 1'S) isomer as a white solid (32 mg, 28%).

'H NMR (MeOD): B/ppm 8.24 (2H, d, J = (2H, d, J = 8.5), 7.95-7.56 (1 H, m), 5.49-5.36 (1 H, m), 3.86-3.36 (2H, m), 3.17 (3H, s), 3.15-2.80 (1H, m), 1.61-1.04 (6H, m), 1.04-0.90 (9H, m) and 0.84-0.78 (3H, m).

"C NMR (MeOD): 8/ppm (rotamers) 201.2,201.1,176.9,176.6,175.6,146.3,144.3, 2,44.5, 42.0,36.0,35.8,32.4,31.6,30.5,30.0,28.7,28.4,24.0 and 14.6.

LRMS: (m/z) 463 (M + Na) +, 441 (M + H) +; 439 (M-H)-.

HPLC: 82%.

MIC (E. coll): 6.25 pM MIC (S. capitis): 25 AM Example 17<BR> <BR> 3-Cyclopentyl-2 (S)- [ (N-formyl-N-hydroxyamino)-methyl]-N- [1' (R)- (4- methoxybenzoyl)-2', 2'-dimethyl propyl] propionamide [Enantiomer of Example 5] The title compound was prepared in an analogous manner to Example 5 as described in Scheme 1 utilising D-t-leucine in Step A and 2 (S)- (benzyloxyamino-methyl)-3-cyclopentyl-propionic acid in Step E. 2 (S)- (benzyloxyamino-methyl)-3- cyclopentyl-propionic acid was synthesised in an analogous manner to 2 (R)- (benzyloxyamino-methyl)-3-cyclopentyl-propionic acid using (R)- (+)-4-benzyl-2- oxazolidinone as the chiral auxilliary.

Spectral data was consistent with Example 5.

MIC (E. coll): 100 μM MIC (S. capitis): 25 μM Example 18 2(R)-[(N-Formyl-N-hydrocyamino)-methyl]-hexanoicacid-(1'(S)-(furan-2-carbonyl)- 2', 2'-dimethylpropyl) amide The title compound was prepared from furan in an analogous manner to that described in Scheme 2, using 2-lithiofuran in Step C. The relevant spectroscopic data are described below.

STEP C: 2 (R)-(N-Benzyioxyaminomethyl)-hexanoic acid-(1'(S)-(furan-2-carbonyl)- 2',2'-dimethylpropyl)amide.

Purification by column chromatography (SiO2,5: 1 iso-hexane: ethyl acetate) gave the product as a colourless oil (75 mg, 37%).

'H NMR (CDCI3): 8/ppm 7.69-7.63 (1 H, m), 7.46-7.30 (5H, m), 7.33 (1 H, d, J = 3.5 Hz), 6.98 (1 H, d, J = 9.6 Hz), 6.57 (1H, dd, J = 3.5,1.7 Hz), 5.72 (1H, brs), 5.34 (1H, d, J = 9.6 Hz), 4.75 (2H, s), 3.22-3.01 (2H, m), 2.60-2.44 (1H, m), 169-1.50 (1H, m), 1.50-1.34 (1 H, m), 1.34-1.12 (4H, m), 1.01 (9H, s), 1.84 (3H, t, J = 6.8 Hz).

LRMS: (m/z) 414.8 (M+H) +.

STEP D: 2 (R)-[(N-Benzyloxy-N-formylamino) methyl]-hexanoic acid-(1'(S)-(furan-2- carbonyl)-2',2'-dimethylpropyl)amide.

Purification by column chromatography (SiO2,4: 1 to 2: 1 iso-hexane: ethyl acetate) gave the product as a colourless oil (70 mg, 87%).

'H NMR (CDCI3): 6/ppm 8.04 (0.6H, brs), 7.90 (0.4H, brs), 7.65 (1 H, d, J = 1.7 Hz), 7.52-7.32 (5H, m), 7.32 (1H, d, J = 3.5 Hz), 6.28 (1H, dd, J = 3.5,1.7 Hz), 6.29 (1 H, d, J = 9. 3 Hz), 5.27 (1H, d, J = 9.2

Hz), 5.10-4.90 (1H, m), 4.90-4.72 (1H, m), 3.87- . 3.58 (2H, m), 3.20-3.01 (1 H, m), 2.74-2.50 (1 H, m), 1.65-1.46 (2H, m), 1.46-1.06 (4H, m), 0.95 (9H, s), 0.80 (3H, t, J = 6.8 Hz).

LRMS: (m/z) 423.2 (M+H) +, 465.2 (M+Na) +.

STEP E: 2 (R)- [ (N-formyl-N-hydroxyamino) methyl]-hexanoic acid- (l' (S)- (furan-2 carbonyl)-2', 2'-dimethylpropyl) amide.

The title compound was isolated as a white crystalline solid (50 mg, 84%).

'H NMR (CD30D): #/ppm 8.35 (0.6H, d, J = 8.8 Hz), 8.26 (0.2H, s), 8.24 (0.4H, d), 7.89-7.82 (1.8H, m), 7.46 (1 H, d, J = 3.6 Hz), 6.67 (1 H, dd, J = 7 Hz), 5.28- 5.20 (1 H, m), 3.85-3.70 (1 H, m), 3.61 (0.4H, dd, J = 14.0,5.5 Hz), 3.41 (0.6H, dd, J = 14.2,4.6 Hz), 3.12-2.98 (0.6H, m), 2.96-2.82 (0.4H, m), 1.57-1.36 (2H, m), 1.36- 1.12 (4H, m), 1.00 (3.6H, s), 0.99 (5.4H, s), 0.80 (3H, t, J = 6.9 Hz).

'3C NMR (CD30D): b/ppm 2, 6.

LRMS: (m/z) 353.2 (M+H) +, 375.2 (M+Na) +, 351.2 (M-H)-.

MIC (E. coli): 12. 5 µM MIC (S. capitis): 12. 5 µM Example 19 2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(2', 2'-dimethyl-1'(S)-(1- methyl-1 H-pyrrole-2-carbonyl)-propyl) amide The title compound was prepared from 1-methylpyrrole in an analogous manner to that described in Scheme 5, using 2-lithio-1-methylpyrrole in Step A. The relevant spectroscopic data are described below.

STEP B: [2,2-dimethyl-1 (S)- (1-methyl-1 H-pyrrole-2-carbonyl)-propyl]-carbamic acid tert-butyl ester.

Purification by column chromatography (SiO2,18: 1 iso-hexane: ethyl acetate) gave the product as an orange oil (0.18 g, 80%).

'H NMR (CDCI3): #/ppm 7.19-7.12 (1H, m), 6.90-6.84 (1H, m), 6.19-6.12 (1H, m), 5.48 (1 H, d, J = 9. 6 Hz), 4.82 (1H, d, J = 9.6 Hz), 3.94 (3H, s), 1.44 (9H, s), 0.98 (9H, s).

LRMS: (m/z) 295.2 (M+H) +.

STEP C: 2 (S)-Amino-3,3-dimethyl-1- (1-methyl-1H-pyrrol-2-yl)-butan-1-one hydrochloride.

The title compound was isolated as a pale purple solid and used without further purification (0.13g, 100% crude).

'H NMR (CD. OD) : 6/ppm 7.15-7.08 (1H, m), 6.93-6.87 (1 H, m), 6.18-6.10 (1 H, m), 4.61 (1 H, brs), 3.93 (3H, s), 1.02 (9H, s).

LRMS: (m/z) 195.0 (M+H) +.

STEP D: 2 (R)-[(N-Benzyloxy-N-formylamino)methyl]-hexanoic acid-(2',2'-dimethyl- 1' (S)- (1-methyl-1 H-pyrroie-2-carbonyl)-propyl) amide.

. Purification by column chromatography (SiO2,4: 1 to 1: 1 iso-hexane: ethyl acetate) gave the product as a pale brown oil (0.16 g, 68%).

'H NMR (CDC13): #/ppm 8.13 (0.6H, brs), 7.92 (0.4H, brs), 7.56-7.28 (5H, m), 7.21- 7.12 (1H, m), 6.92-6.83 (1 H, m), 6.31 (1 H, d, J = 9. 7 Hz), 6.25 (1H, dd, J = 3.8,2.6 Hz), 5.17 (1H, d, J = 9.7 Hz), 5.08-4.91 (1H, m), (1 H, m), 3.92 (3H, s), 3.89-3.54 (2H, m), 3.19-3.02 (1H, m), 2.64-2.48 (1H, m), 1.64-1.32 (2H, m), 1.32- 1.07 (4H, m), 0.96 (9H, s), 0.80 (3H, t, J = 7. 0 Hz).

LRMS: (m/z) 456.2 (M+H) +, 478.2 (M+Na) +.

STEP E: 2 (R)[(N-formyl-N-hydroxyamino)methyl]-hexanoic acid-(2',2'-dimethyl- 1' (S)- (1-methyl-1 H-pyrrole-2-carbonyl)-propyl) amide.

The title compound was isolated as a pale brown crystalline solid (60 mg, 80%).

'H NMR (CD30D): â/ppm 8.26 (0.5H, brs), 8.18 (0.5H, d, J = 9.4 Hz), 8.07 (0.5H, brd, J = 10.1 Hz), 7.85 (0.5H, s), 7.19 (1H, d, J = 3.8 Hz), 7.10-7.00 (1H, m), 6.15 (1 H, dd, J = 3.7,2.4 Hz), 5.25-5.15 (1H, m), 3.90 (3H, s), 3.88-3.71 (1H, m), 3.70- 3.52 (0.5H, m), (0.5H obs. by CD30D peak), 3.11-2.92 (0.5H, m), 2.92-2.76 (0.5H, m), 1.63-1.31 (2H, m), 1.31-1.05 (4H, m), 0.99 (4.5H, s), 0.97 (4.5H, s), 0.76 (3H, t, J = 6.8 Hz).

"C NMR (CD30D): #/ppm 4,176.1,134.5,132.7,122.9,109.7,61.9, 6,28.1,24.0,14.6.

LRMS: (m/z) 366.2 (M+H)', 388.2 (M+Na) +, 363.8 (M-H)-.

MIC (E. coli): 12. 5 µM MIC (S. capitis): 12. 5 µM Example 20 2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoicacid-(1'(S)-(4-aminobenzoly)- 2', 2'-dimethylpropyl) amide The title compound was prepared in as described in Scheme 11, using the General Protocol (GP) thereafter. The experimental details of the synthesis and relevant spectroscopic data are described below. /F/NHz NH p AN I Step B31-1 \ 0" H 0 Reagents and Conditions: A.DMF B. Benzyl chloroformate, pyridine, DCM Scheme 11 STEP A: [1 (S)- (4-Aminobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyi ester.

Sodium azide (1.26 g, 19.4 mmol) was added to a solution of [1 (S)- (4- fluorobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester (0.20 g, 0.7 mmol) in DMF (15 mL), and the mixture heated at 120 °C for 40 hours. The solvent was removed in vacuo before addition of 10% NaHC03 (aq.) (30 mL) to the residual solid. The aqueous phase was extracted with ethyl acetate (2 x 30 mL) and the organic phases washed with brine (1 x 30 mL), dried over MgSO4, filtered and the solvent removed in vacuo to give a yellow solid. Purification by column chromatography (SiO2,4: 1 iso-hexane: ethyl acetate) afforded the title compound as a yellow solid (67 mg, 36%).

'H NMR (CDCI3): 6/ppm 7.85 (2H, d, J = 8.5 Hz), 6.65 (2H, d, J = 8.6 Hz), 5.45 (1 H, brd, J = 9.2 Hz), 5.08 (1H, d, J = 9.6 Hz), 4.17 (2H, brs), 1.42 (9H, s), 0.93 (9H, s).

LRMS: (m/z) 329.2 (M+Na) +.

STEP B: [4- (2 (S)-tert-Butoxycarbonylamino-3, 3-dimethylbutyryl)-phenyl]-carbamic acid benzyl ester.

A solution of [1 (S)- (4-aminobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester (67 mg, 0.22 mmol) and triethylamine (95 µL, 0.69 mmol) in DCM (3 mL) was cooled on an ice bath prior to addition of benzyl chloroformate (98 L, 0.69 mmol).

The reaction was warmed to room temperature and left for 15 hours. Examination by T. I. c. suggested minimal conversion to product hence pyridine (0.10 mL, 1.2 mmol) was added and the reaction left for a

further 2 hours. Solvent was removed in vacuo and the residue taken up in ethyl acetate (20 mL). The organic phase was washed . with 1 M HCI (1 x 20 mL), brine (1 x 20 mL), 1 M Na2CO3 (1 x 20 mL) and brine (1 x 20 mL, dried over MgSO4, filtered and the solvent removed in vacuo, giving a yellow solid. Purification by column chromatography (SiO2,9: 1 iso-hexane: ethyl acetate) afforded the title compound as a yellow solid (90 mg, 90%).

'H NMR (CDCI3): #/ppm 7.77 (1 H, d, J = 8.7 Hz), 7.50 (1 H, d, J = 8.7 Hz), 7.42-7.32 (5H, m), 7.00 (1H brs), 5.43 (1H, brd, J = 9. 5 Hz), 5.22 (2H, s), 5.12 (1H, d, J = 9.7 Hz), 1.42 (9H, s), 0.91 (9H, s).

LRMS: (m/z) 463.2 (M+Na)', 439.2 (M-H)-.

STEP GPA: [4- (2 (S)-amino-3,3-dimethylbutyryl)-phenyl]-carbamic acid benzyl ester hydrochloride.

The title compound was isolated as a foam and used without further purification (75 mg, 100% crude).

'H NMR (CDCl3) : 6/ppm 8.88 (0.5H, brs), 8.41-8.21 (3H, m), 7.59-7.50 (2.5H, m), 7.30-7.21 (2H, m, obs. by CDCI3 peak), 7.432-7.31 (5H, m), 7.00 (1 H brs), 4.86-4.68 (1 H, m), 5.15 (2H, s), 1.04 (9H, s).

LRMS: (m/z) 341.2 (M+H) +, 363.2 (M+Na) +.

STEP GPB: [4-(2 (S)-{2 (R)-(N-Formyl-N-hydroxyamino)-methyl]-hexanoylamino}-3,3-dimethylbutyryl)-phenyl]-carbamic acid benzyl ester.

Purification by column chromatography (SiO2,4: 1 iso-hexane: ethyl acetate) afforded the title compound as a pale brown oil (50 mg, 42%).

'H NMR (CDCl3) : â/ppm 8.13 (0.4H, brs), 8.04-7.80 (2.6H, m), 7.78-7.52 (1H, m), <BR> <BR> <BR> <BR> 7.57 (2H, d, J = 8.7), 7.45-7.28 (10H, m), 6.38 (1 H, d, J = 9.3 Hz), 5.46 (1 H, d, J = 9.3 Hz), 5.20 (2H, s), 5.08-4.86 (1 H, m), 4.86-4.70 (1 H, m), 3.89-3.54 (2H, m), 2.62- . 2.50 (1 H, m), 1.62-1.27 (2H, m), 1.27-1.05 (4H, m), 0.88 (9H, s), 0.75 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 602.2 (M+H) +, 624.2 (M+Na) +, 600.2 (M-H)-.

STEP GPC: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4- aminobenzoyl)-2', 2'-dimethylpropyl) amide.

The title compound was isolated as a white crystalline solid (29.5 mg, 100%).

'H NMR (CD30D): â/ppm 8.27 (0.3H, s), 8.11 (0.7H, d, J = 9.3 Hz), 8.00 (0.3H, d, J = 9. 4 Hz), 7.86 (0.7H, s), 7.80 (2H, d, J = 8. 8 Hz), 6.65 (2H, d, J = 8. 8 Hz), 5.44 (1H, d, J = 9. 4 Hz), 3.8 (1H, dd, J = 14.2, 9.7 Hz), 3.61 (0.5H, dd, J = 13. 8,5.4 Hz), 3.41 (0.5H, dd, J = 14.2,4.6 Hz), 3.09-2.93 (1 H, m), 1.59-1.30 (2H, m), 1.30-1.03 (4H, m), 0.96 (4.5H, s), 0.95 (4.5H, s), 0.75 (3H, t, J = 6.9 Hz).

"C NMR (CD30D): 7,29.9,53.9,50.3, 0,14.5.

LRMS: (m/z) 400.2 (M+Na) +.

MIC (E. coli) : 6.25 pM MIC (S. capitis): 12.5 pM Example 21 2(R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (2', 2'-dimethyl-1' (S)- [4- (2,2,2-trifluoroacetylamino)-benzoyl]-propyl) amide The title compound was prepared as described in Scheme 12, using the General Procedure (GP)

thereafter. The experimental details of the synthesis and relevant spectroscopic data are described below. O/F O/Ns O/N II C 0 t-a >o 0 No N 0 Hz O O Reagents and Conditions: A. NaN3, DMF, 120°C B. i) H2,10% Pd-C, MeOH, ii) Trifluoroacetic anhydride, pyridine, DCM Scheme 12 STEP A: [1 (S)- (4-Azidobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester.

Sodium azide (37.9 g, 0.58 mol) was added to a solution of [1 (S)- (4-fluorobenzoyl)- 2,2-dimethylpropyl]-carbamic acid tert-butyl ester (6.0 g, 19.4 mmol) in DMF (400 mL), and the mixture heated at 120 °C for 24 hours. The solvent was removed in vacuo and the residual solid taken up in ethyl acetate (200 ml). The organic phase was washed with 1 M Na2CO3 (1 x 400 ml) and brine (1 x 400 mL), dried over MgSO4, filtered and the solvent removed in vacuo to give a yellow solid. Purification by column chromatography (SiO2,6: 1 iso-hexane: ethyl acetate) afforded the title compound as a yellow solid (1.96 g) and [1 (S)- (4-Azidobenzoyl)-2, 2-dimethylpropyl]- carbamic acid tert-butyl ester as an orange solid (0.97 g) (47% combined yield).

'H NMR (CDCI3): B/ppm 8.01 (2H, d, J = 8.7 Hz), 7.09 (2H, d, J = 8.7 Hz), 5.37 (1 H, brd, J = 9. 4 Hz), 5.10 (1 H, d, J=9. 6Hz), 1.43 (9H, s), 0.93 (9H, s).

LRMS: (m/z) 327.2 (M+H)', 355.2 (M+Na) +.

STEP B: 2-trifluoroacetylamino)-benzoyl]-propyl)-carbamic acid tert-butyl ester.

To a degassed solution of [1 (S)- (4-azidobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester (1.0 g, 3.0 mmol) in methanol (10 mL) was added 10% palladium on charcoal (0.20 g). Hydrogen gas was bubbled through the suspension for 15 minutes when a balloon containing hydrogen was introduced to the reaction. After 15 hours, the catalyst was removed by filtration and washed liberally with methanol and DCM. The solvents were removed in vacuo to give a pale cream solid (1.0 g).

The crude material was mixed with DCM (20 mL) and dissolution occurred on addition of triethylamine (0.63 mL, 3.16 mmol). The mixture was cooled to 0°C (ice bath) and trifluoroacetic anhydride (0.45 mL, 3.16 mmol) was added dropwise. After 2 hours, further triethylamine (0.3 mL, 2.2 mmol) and trifluoroacetic anhydride (0.30 mL, 2.11 mmol) were added and the reaction proceeded for a further 2 hours. The solvent was removed in vacuo and ethyl acetate (20 mL) added to the residue. The organic phase was washed with 10% citric acid (aq.) (1 X 40 mL) and brine (1 x 40 mL), dried over MgSO4, filtered and the solvent removed in vacuo to give a brown oil. Purification by column chromatography (SiO2,9: 1 iso-hexane : ethyl acetate) afforded the title compound as a pale brown oil (0.63 g, 52%).

'H NMR (CDCI3): 6/ppm 8.58 (1 H, brs), 8.00 (2H, d, J = 8.6 Hz), 7.69 (2H, dd, J = 8.5,1.9 Hz), 5.42 (1H, brd, J = 9.4 Hz), 5.10 (1H, d, J = 9. 5 Hz), 1.43 (9H, s), 0.93 (9H, s).

LRMS: (m/z) 425.2 (M+Na) +.

STEP GPA: N- [4- (2 2-trifluoroacetamide.

. The title compound was recovered as a pale brown solid and used without further purification (0.55 g, 100% crude).

'H NMR (CD30D): 5/ppm 8.12 (2H, d, J = 8.8 Hz), 7.90 (2H, d, J = 8.8 Hz), 5.04 (1 H, s), 1.05 (9H, s).

LRMS: (m/z) 303.2 (M+H) +, 325.2 (M+Na) +.

STEP GPB: 2 (R)-[(N-Benzyloxyl-N-formylamino)-methyl]-hexanoic acid-(2', 2'- dimethyl-1'(S)-[4-(2,2,2-trifluoroacetylamino)-benzoyl]-propyl)-amide.

Purification by column chromatography (SiO2,8: 1 iso-hexane: ethyl acetate) afforded the title compound as a pale brown oil (0.4 g, 44%).

'H NMR (CDCI3): b/ppm 9.03 (1H, brs), 8.13 (0.6H, brs), 8.00 (2H, d, J = 8.7), 7.91 (0.4H, brs), 7.72 (2H, d, J = 8.8), 7.43-7.32 (5H, m), 6.36 (1H, d, J = 8.9 Hz), 5.42 (1 H, d, J = 9.0 Hz), 5.08-4.90 (1 H, m), 4.90-4.74 (1 H, m), 3.95-3.75 (1 H, m), 3.75- 3.58 (1 H, m), 2.68-2.55 (1 H, m), 1.62-1.30 (2H, m), 1.30-1.05 (4H, m), 0.88 (9H, s), 0.78 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 564.2 (M+H) +, 686.2 (M+Na) +.

STEP GPC : 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl-hexanoic acid-(2',2'-dimethyl- 1'(S)- [4-(2,2,2-trifluoroacetylamino)-benzoyl]-propyl) amide Purification by reverse phase preparative HPLC yielded the title compound as a white glassy solid (20 mg, 50%).

'H NMR (CDCI3): ã/ppm 8.27 (0.3H, s), 8.06 (2H, d, J = 8.7 Hz), 7.90-7.78 (2.7H, m), 5.46 (1H, s), 3.88-3.72 (1H, m), 3.61 (0.3H, dd, J = 14.2,5.8 Hz), 3.42 (0.7H, dd, J = 14.1,4.3 Hz), 3.10-2.96 (0.7H, m), 2.95-2.80 (0.3H, m), 1.59-1.30 (2H, m), 1.30-1.04 (4H, m), 0.99 (3H, s), 0.98 (6H, s) and 0.75 (3H, t, J = 6.9 Hz).

'C NMR (CDCl3) : b/ppm 0,176.7,176.4,157.3 (q, J = 38 Hz), 2,122.0,117.7 (q, J = 288 Hz), 1,31.6,30.5, 0,14.5.

LRMS: (m/z) 474.2 (M+H) +, 496.2 (M+Na) +, 472.2 (M-H)-.

MIC (E. coll9: 6. zip MIC (S. capitis): 6.25 fJvt Example 22 2(R)-[(N-formyl-N-hyxroxyamino)-methyl]-hexanoicacid-(1'(S)-(4- acetylaminobenzoyl)-2', 2'-dimethylpropyl) amide The title compound was prepared from 2 (R)-[(N-benzyloxyl-N-formylamino)-methyl]- hexanoic acid-(2',2'-dimethyl-1'(S)-[4-(2, 2,2-trifluoroacetylamino)-benzoyl]-propyl)- amide as described in Scheme 13. The experimental details of the synthesis and relevant spectroscopic data are described below. /N/CF3 0/NHZ il StopA N p O NOBn NOBn O ; H O+H H zizis Step B \ 0 O \ U OAH O H I y im H H O"H 0'_H Reagents and Conditions: A.(aq.),MeOHNa2CO3 B. Acetic anhydride, pyridine, DCM C. H2, 10% Pd-C, MeOH Scheme 13 STEP A: 2 (R)-[(N-Benzyloxyl-N-formylamino)-methyl]-hexanoic acid-(1'(S)-(4-aminobenzoyl]-2', 2'-dimethylpropyl)-amide.

To a solution of 2 (R)-[(N-benzyloxy-N-formylamino)-methyl]-hexanoicx acid-(2', 2'- dimethyl-1' (S)-[4- (2,2,2-trifluoroacetylamino)-benzoyl]-propyl)-amide (0.35 g, 0.62 mmol) in methanol (4 mL) was added 1 M Na2CO3. The reaction was left at room temperature for 4 hours when the mixture was extracted with ethyl acetate (2 x 20 mL). The organic phases were washed with brine (1 x 20 mL) and dried over MgSO4, filtered and the solvent removed in vacuo. The resulting foam was purified by column chromatography (SiO2,4: 1 iso-hexane: ethyl acetate) afforded the title compound as a pale brown oil (0.23 g, 79%).

'H NMR (CDCl3) : ã/ppm 9.03 (1H, brs), 8.13 (0.6H, brs), 7.91 (0.4H, brs), 7.85 (2H, d, J=8. 67), 7.46-7.32 (5H, m), 6.64 (2H, d, J=8. 7), 6.38 (1H, d, J=9. 3Hz), 5.43 (1 H, d, J = 9.4 Hz), 5.09-4.90 (1 H, m), 4.90-4.74 (1 H, m), 3.90 (2H, m), 2.62-2.48 (1H, m), 1.612-1.28 (2H, m), 1.28-1.03 (4H, m), 0.90 (9H, s), 0.76 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 468.2 (M+H) +, 490.2 (M+Na) +, 466.4 (M-H)-.

STEP B: 2 (R)-[(N-Benzyloxyl-N-formylamino)-methyl]-hexanoic acid-(1'(S)-(4- acetylaminobenzoyl]-2',2'-dimethylpropyl)-amide.

A solution of 2 (R)-[(N-benzyloxyl-N-formylamino)-methyl]-hexanoic acid-(1'(S)-(4- aminobenzoyl]-2', 2'-dimethylpropyl)-amide (0.1 g, 0.21 mmol) in DCM (2 mL) was cooled to 0°C (ice bath) before addition of pyridine (34.6 J, 0.43 mmol) and acetyl chloride (30.5 pI, 0.43 mmol). The reaction was warmed to room temperature and left for 15 hours. The solvent was removed in vacuo and the residue dissolved in ethyl acetate (10 mL). The organic phase was washed with brine (1 x 20 mL), dried over MgS04, filtered and the solvent removed in vacuo, affording a pale brown oil which was used without further purification (0.11 g, 100% crude).

'H NMR (CDCl3) : 6/ppm 8.13 (1 H, brs), 7.96 (2H, d, J = 8.7), 7.82 (1 H, brs), 7.62 (2H, d, J = 8.8), 7.43-7.32 (5H, m), 6.37 (1 H, d, J = 9.2 Hz), 5.45 (1 H, d, J = 9.3 Hz), 5.08-4.90 (1 H, m), 4.90-4.74 (1 H, m), 3.92-3.58 (2H, m), 2.66-2.52 (1 H, m), 2.20 (3H, s), 1.62-1.30 (2H, m), 1.30-1.05 (4H, m), 0.88 (9H, s), 0.78 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 510.4 (M+H) +, 532.4 (M+Na) +.

STEP C: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4- acetylaminobenzoyl)-2', 2'-dimethylpropyl) amide.

To a degassed solution of 2 (R)-[(N-benzyloxyl-N-formylamino)-methyl]-hexanoic acid- (1' (S)- (4-acetylaminobenzoyl]-2', 2'-dimethylpropyl)-amide (0.11 g, 0.21 mmol) in methanol (2 mL) was added 10% palladium on charcoal (20 mg). Hydrogen gas was bubbled through the suspension for 10 minutes when a balloon containing hydrogen was introduced to the reaction. After 2 hours, the catalyst was removed by filtration and the solvents were removed in vacuo to give a pale brown solid.

Purification by reverse phase preparative HPLC afforded the title compound as a #white crystalline solid (54 mg, 61%).

'H NMR (CD30D): 8/ppm 8.30 (0.6 H, d, J = 9.1 Hz), 8.27 (0.4H, s), 8.19 (0.4H, d, J = 9.1 Hz), 7.99 (2H, d, J = 8.8 Hz), 7.86 (0.6H, s), 7.71 (2H, d, J = 8.8 Hz), 5.47 (1H, d, J = 9.1 Hz), 3.88-3.72 (1H, m), 3.61 (0.3H, dd, J = 13.9,5.7 Hz), 3.41 (0.7H, dd, J = 14.1,4.6 Hz), 3.09-2.95 (0.7H, m), 2.95-2.80 (0.3H, m), 2.15 (3H, s), 1.59-1.30 (2H, m), 1.30-1.04 (4H, m), 0.96 (9H, s), 0.74 (3H, t, J = 7.0 Hz).

"C NMR (CD30D): 5/ppm 8,131.3, 8,53.9,50.3,4537,45.5,36.2,31.6,30.6,27.9,24.5,34.0,14.5.

LRMS: (m/z) 420.2 (M+H) +, 442.2 (M+Na)+, 418.4 (M-H)-.

MIC (E. colza: 12.5 s1M MIC (S. capitis): 3.1 1M Example 23 2(R)-[(N-Formyl-N-hyd roxyamino)-methyl]-hexanoic acid-(1'(S)-(4- methanesulfonylaminobenzoyi)-2', 2'-dimethylpropyl) amide The title compound was prepared in an analogous manner to 2 (R)-[(N-formyl-N- hydroxyamino)-methyl]-hexanoic acid- (1' (S)- (4-acetylaminobenzoyl)-2', 2'- dimethylpropyl) amide as described in Scheme 13, using methanesulfonyl chloride in Step B. The relevant spectroscopic data are described below.

STEP B: 2 (R)- [ (N-Benzyloxyl-N-formylamino)-methyl]-hexanoic acid- (1' (S)- (4-methanesulfonylaminobenzoyl]-2', 2'-dimethylpropyl)-amide.

The title compound was afforded as a pale brown oil and used without further purification (0.10 g, 91% crude).

'H NMR (CDCl3) : 5/ppm 8.29 (1H, s), 8.15 (0.5H, brs), 8.03-7.94 (2.5H, m), 7.82 (1H, brs), 7.62 (2H, d, J = 8.8), 7.45-7.32 (7H, m), 6.45 (1H, d, J = 9. 2 Hz), 5.46 (1H, d, J = 9.3 Hz), 5.10-4.90 (1H, m), 4.90-4.76 (1H, m), 4.04-3.84 (1H, m), 3.82-3.62 (1H, m), 3.69 (3H, s), 2.70-2.57 (1 H, m), 1.62-1.32 (2H, m), 1.32-1.05 (4H, m), 0.90 (9H, s), 0.77 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 546.2 (M+H)+, 568.2 (M+Na) +.

STEP C: 2 (R)-[(N-Formyi-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4-methanesulfonylaminobenzoyl)-2', 2'-dimethylpropyl) amide Purification by reverse phase preparative HPLC afforded the title compound as a pale brown crystalline solid (30 mg, 31 %).

'H NMR (CD30D): ã/ppm 8.30 (0.4 H, d, J = 9.2 Hz), 8.27 (0.4H, s), 8.19 (0.6H, d, J = 8. 7 Hz), 8.02 (2H, d, J = 8.8 Hz), 7.86 (0.6H, s), 7.33 (2H, d, J = 8.8 Hz), 5.46 (1 H, d, J = 9. 0 Hz), 3.87-3.72 (1H, m), 3.61 (0.3H, dd, J = 14.1,5.7 Hz), 3.42 (0.7H, dd, J = 14.2,4.6 Hz), 3.06 (3H, s), 3.09-2.95 (0.7H, m), 2.95-2.80 (0.3H, m), 1.59-1.30 (2H, m), 1.30-1.02 (4H, m_, 0.98 (3H, s), 0.97 (6H, s), 0.76 (3H, t, J = 7.0 Hz).

"C NMR (CD30D): #/ppm 8,145.2,134.7,131.9, 6.

LRMS: (m/z) 456.2 (M+H) +, 478.2 (M+Na) +, 454.4 (M-H)-.

MIC (E. coll9: 50 µM MIC (S. capitis): 3.1 µM Example 24 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(2', 2'-dimethyl-1'(S)- (4- morpholin-4-ylbenzoyl)-propyl) amide The title compound was prepared in as described in Scheme 14, foliowed by the General Protocol (GP). The experimental details of the synthesis and relevant spectroscopic data are described beiow. 0 ! rj XJ step A o N J H O O H II v O Reagents and Conditions: A. Morpholine, DMSO, Et, N, 1200C Scheme 14 STEP A: [2,2-Dimethyl-1 (S)- (4-morpholin-4-ylbenzoyl)-propyl]-carbamic acid tert- butyl ester.

Morpholine (1.41 mL, 16.2 mmol) and triethylamine (0.25 mL, 1.8 mmol) were added to a solution of [1 (S)- (4-fluorobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester (0.5 g, 1.62 mmol) in DMSO (8 mL), and the mixture heated at 120 °C for 15 hours. The solvent was removed in vacuo and the residual solid taken up in ethyl acetate (30 ml), and washed with 10% citric acid (aq.) (1 x 40 ml). The aqueous layer re-extracted with ethyl acetate (1 x 30 mL) and the combined organic phases were washed with brine (1 x 40 mL), dried over MgSO4, filtered and the solvent removed in vacuo to give a pale brown oil which was used without further purification (0.63 g, 100% crude).

'H NMR (CDCL): B/ppm 7.95 (2H, d, J = 9.0 Hz), 6.88 (2H, d, J = 9.0 Hz), 5.46 (1 H, brd, J = 9.6 Hz), 5.10 (1 H, d, J = 9.7 Hz), 3.90-3.82 (4H, m), 3.38-3.28 (4H, m), 1.42 (9H, s), 0.93 (9H, s).

LRMS: (m/z) 377.2 (M+H)+, 399.2 (M+Na) +.

STEP GPA: 2 (S)-Amino-3,3-dimethyl-1- (4-morpholin-4-yiphenyl)-butan-1-one.

The title compound was recovered as pale brown solid and used without further . purification (0.52 g, 100% crude).

'H NMR (CDCL): 6/ppm 8.06 (2H, d, J = 9.0 Hz), 7.31 (2H, d, J = 9.0 Hz), 4.96 (1 H, s), 3.99-3.89 (4H,

m), 3.55-3.45 (4H, m), 1.04 (9H, s).

LRMS: (m/z) 277.2 (M+H)+, 299.2 (M+Na) +.

STEP GPB: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(2', 2'- dimethyl-1' (S)- (4-morpholin-4-ylbenzoyl)-propyl)-amide Purification by column chromatography (SiO2,2: 1 to 2: 3 iso-hexane: ethyl acetate) afforded the title compound as a pale brown oil (0.63 g, 72%).

'H NMR (CDCI3): B/ppm 8.13 (0.6H, brs), 8.98-7.88 (0.4, m), 7.94 (2H, d, J = 8.8 Hz), 7.48-7.30 (5H, m), 6.86 (2H, d, J = 9.0), 6.36 (1H, d, J=9. 3Hz), 5.46 (1H, d, J = 9.4 Hz), 5.10-4.90 (1H, m), 4.90-4.75 (1 H, m), 3.90-3.80 (4H, m), 3.90-3.53 (2H, m), 3.38-3.28 (4H, m), 2.62-2.50 (1 H, m), 1.60-1.30 (2H, m), 1.30-1.02 (4H, m), 0.90 (9H, s), 0.76 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 538.4 (M+H) +, 560.4 (M+Na) +, 536.4 (M-H)-.

STEP GPC: 2 (R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (2', 2'-dimethyl- 1' (S)- (4-morpholin-4-ylbenzoyl)-propyl) amide Purification by reverse phase preparative HPLC yielded the title compound as a pale beige foam (0.36 g, 69%).

'H NMR (CD30D): 6/ppm 8.27 (0.3 H, s), 7.93 (2H, d, J = 9.0 Hz), 7.85 (0.7H, s), 6.97 (2H, d, J = 9.1 Hz), 5.46 (1 H, s), 3.88-3.73 (5H, m), 3.61 (0.3H, dd, J = 13.8, 5.8 Hz), 3.41 (0.7H, dd, J = 6 Hz), 3.39-3.27 (4H, m), 3.09-2.92 (0.7H, m), 2.92-2.78 (0.3H, m), 1.57-1.28 (2H, m), 1.28-1.00 (4H, m), 0.97 (3H, s), 0.95 (6H, s), 0.74 (3H, t, J = 7.0 Hz).

"C NMR (CD30D): â/ppm 8,156.7,132.3,129.4,114.8, 6,27.9,24.0,14.6.

LRMS: (m/z) 448.2 (M+H)+, 470.2 (M+Na)+, 446.4 (M-H)-.

MIC (E. co//): 6.25 µM MIC (S. capitis): 3.1, uM Example 25 2 (R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (1' (S)- [4- (4- benzylpiperazin-1-yl)-benzoyl]-2', 2'-dimethylpropyl) amide The title compound was prepared utilising 1-benzylpiperazine in Step A as described in Scheme 14, and using the General Protocol (GP) thereafter. The relevant spectroscopic data are described below.

STEP A: [1 (S)- [4- (4-Benzylpiperazin-1-yl)-benzoyl]-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester.

1-Benzyloxycarbonyl piperazine (0.45 g, 2.03 mmol) Purification by column . chromatography (SiO2,5: 1 iso-hexane: ethyl acetate) afforded the title compound as a yellow oil (0.68 g, 82%). <BR> <BR> <BR> <BR> <BR> <BR> <P> 'H NMR (CDCI3): 8/ppm 7.91 (2H, d, J = 8.9 Hz), 7.38-7.28 (5H, m), 6.84 (2H, d, J = 9.1 Hz), 5.46 (1H, brd, J = 9. 4 Hz), 5.10 (1H, d, J=9. 6Hz), 3.56 (2H, s), 3.41-3.33 (4H, m), 3.62-3.55 (4H, m), 1.42 (9H, s), 0.93 (9H, s).

LRMS: (m/z) 466.2 (M+H) +, 488.2 (M+Na) +.

STEP GPA: 2 (S)-1- [4- (4-Benzylpiperazin-1-yl)-phenyl]-3, 3-dimethyl-butan-1-one dihydrochloride The title compound was recovered as an orange foam and used without further purification (0.12 g, 100% crude).

'H NMR (CD30D): 8/ppm 8.00 (2H, d, J = 9.0 Hz), 7.66-7.58 (2H, m), 7.54-7.47 (3H, m), 7.11 (2H, d, J = 9.0 Hz), 4.92 (1 H, s), 4.44 (2H, s), 4.25-4.12 (2H, m), 3.62-3.51 (2H, m), 3.40-3.26 (4H, m), 1.03

(9H, s).

LRMS: (m/z) 366.2 (M+H) +, 388.2 (M+Na) +.

STEP GPB: 2 (R)- [ (N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid- (1' (S)- [4- (4-benzylpiperazin-1-yl)-benzoyl]-2', 2'-dimethytpropyl) amide Purification by column chromatography (SiO2, 2: 1 ethyl acetate: iso-hexane) afforded the title compound as a pale yellow oil (37 mg, 24%).

'H NMR (CDCI3): 6/ppm 8.13 (0.6H, brs), 7.98-7.87 (0.4, m), 7.93 (2H, d, J = 8.8 Hz), 7.48-7.30 (5H, m), 6.85 (2H, d, J = 9.0), 6.35 (1H, d, J = 9. 3 Hz), 5.45 (1H, d, J = 9.3 Hz), 5.10-4.90 (1H, m), 4.90-4.75 (1H, m), 3.87-3.58 (2H, m), 3.56 (2H, s), 3.42-3.31 (4H, m), 2.63-2.50 (5H, m), 1.62-1.28 (2H, m), 1.28-1.05 (4H, m), 0.90 (9H, s), 0.76 (3H, t, J = 6. 9 Hz).

LRMS: (m/z) 663.4 (M+Na) +.

STEP GPC: 2 (R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (1' (S)- [4- (4-benzylpiperazin-1-yl)-benzoyl]-2', 2'-dimethylpropyl) amide trifluoroacetic acid Purification by reverse phase preparative HPLC afforded the title compound as a colourless crystalline solid (10 mg, 27%).

'H NMR (CD30D): 6/ppm 8.26 (0.4 H, s), 8.24 (0.3H, d, J = 9.8 Hz), 8.13 (0. 3H, d, J = 9.1 Hz), 7.97 (2H, d, J =8.9 Hz), 7.84 (0.6H, s), 7.59-7.48 (5H, m), 7.06 (2H, d, J = 8.9 Hz), 5.46 (0.5H, d, J = 5.6 Hz), 5.45 (0.5H, d, J = 9.1 Hz), 4.42 (2H, s), 3.79 (1H, dd, J=14.1,8.8 Hz), 3.59 (1H, dd, J = 14.3,5.8 Hz), 3.55-3.26 (8H, m), 3.10-2.95 (0.4H, m), 2.95-2.80 (0.6H, m), 1.56-1.31 (2H, m), 1.31-1.01 (4H, m), 0.96 (4H, s), 0.95 (5H, s), 0.75 (3H, t, J = 6.9).

'3C NMR (CD30D): 5/ppm 199.8,176.3,154.9,132.8,132.3,131.9,131.0,130.9, 5,53.9,52.7,50.3,46.3,45.6,45.5,36.3,31.6,30.6,27.9, 6.

LRMS: (m/z) 533.4 (M+H) +, 559.4 (M+Na) +.

MIC (E. coll9: 50 uM MIC (S. capitis): 3.1 μM Example 26 (4-2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoicacid-(2',2'-dimethyl-1'(S)- piperazin-1-yi-benzoyi)-propyl) amide The title compound was prepared using 1-benzyloxycarbonylpiperazine in Step A as described in Scheme 14, and using the General Protocol (GP) thereafter. The experimental details of the synthesis and relevant spectroscopic data are described below.

STEP A: 4- [4- (2 (S)-tert-Butoxycarbonylamino-3, 3-dimethylbutyryl)-phenyl]- piperazine-1-carboxylic acid benzyl ester Purification by column chromatography (SiO2,5: 1 iso-hexane: ethyl acetate) afforded the title compound as a yellow oil (0.68 g, 82%).

'H NMR (CDCL): 6/ppm 7.93 (2H, d, J = 8.9 Hz), 7.40-7.30 (5H, m), 6.85 (2H, d, J = 9.0 Hz), 5.42 (1 H, brd, J = 8.9 Hz), 5.17 (2H, s), 5.10 (1H, d, J = 9.0 Hz), 3.70-3.62 (4H, m), 3.40-3.32 (4H, m), 1.42 (9H, s), 0.93 (9H, s).

LRMS: (m/z) 332.4 (M+Na) .

STEP GPA: 4- [4- (2 (S)-Amino-3,3-dimethylbutyryl)-phenyl]-piperazine-1-carboxylic acid benzyl ester hydrochloride The title compound was recovered as a red foam and used without further -purification (0.17 g, 100% crude).

'H NMR (CD30D): 5/ppm 8.02 (2H, d, J = 9.0 Hz), 7.51 (2H, d, J = 9.0 Hz), 7.42-7.25 (5H, m), 5.17 (2H, s), 5.05 (1H, s), 3.89-3.79 (4H, m), 3.67-3.52 (4H, m), 1.03 (9H, s).

LRMS: (m/z) 410.2 (M+H) +, 432.2 (M+Na) .

STEP GPB: 4- [4- (2 (S)-12 (R)- [ (N-Benzyloxy-N-formylamino)-methyl]-hexanoylamino)- (3,3-dimethylbutyryl)-phenyl]-piperazine-1-carboxylic acid benzyl ester Purification by column chromatography (SiO2,3: 1 iso-hexane: ethyl acetate) afforded the title compound as a pale yellow oil (0.15 g, 58%).

'H NMR (CDCL): 5/ppm 8.13 (0.6H, brs), 7.95-7.85 (0.4, m), 7.91 (2H, d, J = 8.9 Hz), 7.46-7.29 (5H, m), 6.84 (2H, d, J = 9.0), 6.38 (1 H, d, J = 9.3 Hz), 5.45 (1 H, d, J = 9.4 Hz), 5.17 (2H, s), 5.09-4.90 (1H, m), 4.90-4.75 (1H, m), 3.88-3.60 (6H, m), 3.42-3.31 (4H, m), 2.63-2.49 (1 H, m), 1.62-1.28 (2H, m), 1.28-1.05 (4H, m), 0.90 (9H, s), 0.76 (3H, t, J = 7.0 Hz).

LRMS: (m/z) 671.2 (M+H) +, 693.4 (M+Na) +.

STEP GPC: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(2', 2'-dimethyl- 1' (S)- (4-piperazin-1-yi-benzoyl)-propyl) amide The title compound was recovered as a yellow crystalline solid (0.12 g, 100%).

'H NMR (CD30D): ã/ppm 8.27 (0.3H, s), 7.93 (2H, d, J = 9.0 Hz), 7.85 (0.7H, s), 6.99 (2H, d, J = 9.0 Hz), 5.46 (1H, s), 3.80 (1H, dd, J = 14.1,9.7 Hz), 3.61 (0.5H, dd, J = 13.9,5.7 Hz), 3.48-3.37 (4.5H, m), 3.08-2.96 (4.5H, m), 2.91-2.80 (0.5H, m), 1.57- 1.32 (2H, m), 1.31-1.02 (4H, m), 0.95 (9H, s), 0.75 (3H, t, J = 7.0).

#13C NMR (CD30D): 6/ppm 3,129.4,115.1,60.2, 3,45:8,36.3,31.6,30.6,27.0,24.0,14.6.

LRMS: (m/z) 447.2 (M+H) +, 469.2 (M+Na) +.

MIC (E. coll): 3.1 µM MIC (S. capitis): 12.5 pM Example 27 2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(2', 2'-dimethyl-1'(S)- [4-(4- methylpiperazin-1-yl)-benzoyl]-propyl) amide The title compound was prepared from 4- [4- (2 (S)-tert-butoxycarbonylamino-3,3- dimethylbutyryl)-phenyl]-piperazine-1-carboxylic acid benzyl ester as described in Scheme 15, and using the General Protocol (GP) thereafter. The experimental details of the synthesis and relevant spectroscopic data are described below. I JNZNi CNZ CN Step A O ut I r-a H, r-a Reagents and Conditions: A. H2,10% Pd-C, CH20 (37% wt. % in H20), MeOH Scheme 15 STEP A: {2,2-Dimethyl-1 (S)- [4- (4-methylpiperazin-1-yl)-benzoyl]-propyl}-carbamic acid tert-butyl ester Formaldehyde (37% wt. % solution in H2O, 0.5 mL) was added to a solution of 4- [4- (2(S)-tert-Butoxycarbonylamino-3, 3-dimethylbutyryt)-phenyl]-piperazine-1-carboxylic acid benzyl ester in methanol (3 mL) and ethyl acetate (1 mL). The mixture was degassed and 10% palladium on charcoal (20 mg) was added. Hydrogen gas was bubbled through the suspension for 15 minutes when a balloon containing hydrogen was introduced to the reaction. After 18 hours, the catalyst was removed by filtration and the solvents were removed in vacuo to give a yellow oil which was used without further purification (0.15 g, 100% crude). <BR> <BR> <BR> <BR> <BR> <BR> <P>'H NMR (CDCI3): â/ppm 7.97 (2H, d, J = 8.8 Hz), 7.40-7.30 (5H, m), 6.90 (2H, d, J = 8.9 Hz), 5.44 (1 H, brd, J = 9.6 Hz), 5.09 (1 H, d, J = 9.7 Hz), 3.87-3.78 (4H, m), 3.50- 3.05 (4H, m), 2.85 (3H, s), 1.41 (9H, s), 0.92 (9H, s).

LRMS: (m/z) 390.2 (M+H) I, 402.4 (M+Na) +.

STEP GPA: 2 (S)-Amino-3,3-dimethyl-1- [4- (4-methyipiperazin-1-yt)-phenyl]-butan-1- one.

The title compound was recovered as a yellow foam and used without further purification (0.14 g, 100% crude).

STEP GPB: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(2', 2'- dimethyl-1' (S)- [4-(4-methylpiperazin-1-yl)-benzoyl]-propyl) amide trifluoroaectic acid . Purification by reverse phase preparative HPLC afforded the title compound as a yellow solid (0.15 g, 54%).

'H NMR (CDCl3) : B/ppm 8.13 (0.6H, brs), 8.01-7.91 (0.4, m), 7.95 (2H, d, J = 8.7 Hz), 7.49-7.30 (5H, m), 6.90 (2H, d, J = 8.7), 6.40 (1 H, d, J = 9.0 Hz), 5.44 (1 H, d, J = 9.1 Hz), 5.10-4.90 (1H, m), 4.90-4.74 (1H, m), 4.00-3.33 (8H, m), 3.17-3.79 (2H, m), 2.89 (3H, s), 2.67-2.51 (1H, m), 1.62-1.30 (2H, m), 1.30-1.02 (4H, m), 0.90 (9H, s), 0.76 (3H, t, J = 7.0 Hz).

LRMS: (m/z) 551.2 (M+H) +, 573.4 (M+Na) +.

STEP GPC: 2 (R)-[(N-Formyl-N-hydroxy-amino)-methyl]-hexanoic acid-(2', 2'- dimethyl-1' (S)- [4- (4-methylpiperazin-1-yl)-benzoyl]-propyl) amide trifluoroacetic acid.

Purification by reverse phase preparative HPLC afforded the title compound as a yellow solid (85 mg, 71 %).

'H NMR (CD30D): 8/ppm 8.27 (0.5H, s), 7.98 (2H, d, J = 8.9 Hz), 7.85 (0.5H, s), 7.08 (2H, d, J = 8.9 Hz), 5.46 (1 H, s), 4.25-3.98 (2H, m), 3.80 (1H, dd, J = 14.2,9.0 Hz), 3.71-3.51 (4H, m), 3.42 (1 H, dd, J = 14.2,4.5 Hz), 3.35-3.15 (4H, m), 3.11-2.92 (0.5H, m), 2.97 (3H, s), 2.92-2.81 (0.5H, m), 1.58-1.30 (2H, m), 1.30-1.03 (4H, m), 0.96 (3H, s), 0.95 (6H, s), 0.75 (3H, t, J = 9.9 Hz) "C NMR (CD, OD): 8lppm 3,154.9,132.7,131.0,116.1,60.5, 0,14.6.

LRMS: (m/z) 461.4 (M+H) +.

MIC (E. colt): 6. 25 µM MIC (S. capitis): 6.25 uM Example 28 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(2', 2'-d imethyl-1'(S)- [4-(4- pyrimidin-2-yl-piperazin-1-yl)-benzoyl]-propyl) amide The title compound was prepared from 1- (2-pyrimidyl)-piperazine in Step A as described in Scheme 14, and using the General Protocol (GP) thereafter. The final step yielded both Example 28 and Example 29. Relevant spectroscopic data are described below.

STEP A: {2,2-Dimethyl-1 (S)- [4- (4-pyrimidin-2-ylpiperazin-1-yl)-benzoyl]-propyl}- carbamic acid tert-butyl ester.

Purification by column chromatography (SiO2,5: 2 iso-hexane: ethyl acetate) afforded the title compound as a pale brown oil (0.36 g, 82%).

'H NMR (CDCI3): #/ppm 8.34 (2H, d, J = 4.7), 7.95 (2H, d, J = 8.8 Hz), 6.90 (2H, d, J = 9.0 Hz), 6.54 (1 H, t, J = 4.8), 5.48 (1 H, brd, J = 9.4 Hz), 5.11 (1 H, d, J = 9.7 Hz), 4.04-3.94 (4H, m), 3.54-3.43 (4H, m), 1.42 (9H, s), 0.94 (9H, s).

#LRMS : (m/z) 454.4 (M+H) +.

STEP GPA: 2 (S)-Amino-3, 3-dimethyl-1- [4- (4-pyrimidin-2-ylpiperazin-1-yl)-phenyl]- butan-1-one dihydrochloride.

The title compound was recovered as pale brown solid and used without further purification (0.34 g, 100% crude).

'H NMR (CDOD3): #/ppm 8.67 (2H, d, J = 5.3), 8.00 (2H, d, J = 9.1 Hz), 7.11-7.02 (3H, m), 4.90 (1 H, s), 4.17-4.09 (4H, m), 3.82-3.72 (4H, m), 1.04 (9H, s).

LRMS: (m/z) 354.4 (M+H) +.

STEP GPB: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(2', 2'- dimethyl-l' (S)- [4- (4-pyrimidin-2-ylpiperazin-I-yi)-benzoyl)-propyl)-amide Purification by column chromatography (SiO2,2: 1 to 3: 1 ethyl acetate: iso-hexane) afforded the title compound as a yellow foam (0.24 g, 83%).

'H NMR (CDCl3) : 8/ppm 8.13 (0.6H, brs), 7.98-7.88 (0.4, m), 7.94 (2H, d, J = 8.8 Hz), 7.48-7.30 (5H, m), 6.86 (2H, d, J = 9.0), 6.36 (1H, d, J = 9. 3 Hz), 5.46 (1H, d, J = 9.4 Hz), 5.10-4.90 (1H, m), (1 H, m), 3.90-3.80 (4H, m), 3.90-3.53 (2H, m), 3.38-3.28 (4H, m), 2.62-2.50 (1H, m), 1.60-1.30 (2H, m), 1.30-1.02 (4H, m), 0.90 (9H, s), 0.76 (3H, t, J = 6. 9 Hz).

LRMS: (m/z) 538.4 (M+H) +, 560.4 (M+Na) +, 536.4 (M-H)-.

STEP GPC: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyi]-hexanoic acid-(2', 2'-dimethyl- 1' (S)- [4- (4-pyrimidin-2-yl-piperazin-1-yl)-benzoyl]-propyl) amide Purification by reverse phase preparative HPLC yielded the title compound as a pale yellow glassy solid (65 mg, 34%, 58% combined yield with Example 29).

'H NMR (CD30D): #/ppm 8.34 (2H, d, J = 4.8 Hz), 8.27 (0.3H, s), 7.95 (2H, d, J = 9.0 #Hz), 7.86 (0.7H, s), 7.00 (2H, d, J = 9.0 Hz), 6.61 (1 H, t, J = 4.8 Hz), 5.48 (1 H, s), 3.95 (4H, t, J=5. 3Hz), 3.87-3.73 (1H, m), 3.61 (0.4H, dd, J=14.0,5. 8 Hz), 3.50 (4H, t, J = 5.3 Hz), 3.41 (0.6H, dd, J = 14.0,4.6Hz), 3.09-2.95 (0.6H, m), 2.95-2.78 (0.4H, m), 1.58-1.30 (2H, m), 1.28-1.04 (4H, m), 0.96 (9H, s), 0.74 (3H, t, J = 7.0 Hz).

"C NMR (CD30D): B/ppm 5,156.4,132.4,129.0,
9,60.2,56.9,50.3,45.8,45.6,44.9,36.4,31.6,30.6,28.0,24.0,14.6.

LRMS: (m/z) 525.2 (M+H) +, 547.2 (M+Na) +.

MIC (E. coll): 12.51lM MIC (S. capitis): 1.6 pM Example 29 2 (R)-[(N-Formyl-N-hyd roxyamino)-methyl]-hexanoic acid-(2', 2'-d imethyl-1' (S)- {4- [4- (1,4,5,6-tetrahydropyrimidin-2-yl)-piperazin-1-yl]-benzoyl}-propyl) amide The titre compound was prepared in an identical manner to Example 28 as described in Scheme 14. The final step yielded both Example 28 and Example 29.

Relevant spectroscopic data are described below.

STEP GPC: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(2', 2'-dimethyl- 1' (S)- {4- [4-(1,4,5,6-tetrahydropyrimidin-2-yl)-piperazin-1-yl]-benzoyl}-propyl) amide.

Purification by reverse phase preparative HPLC yielded the title compound as å colourless glassy solid (47 mg, 24%, 58% combined yield with Example 28).

'H NMR (CD30D): 8/ppm 8.27 (0.3 H, s), 7.95 (2H, d, J = 8.9 Hz), 7.86 (0.7H, s), 6.98 (2H, d, J = 8.9 Hz), 5.46 (1 H, s), 3.77 (1 H, dd, J = 14.1,4.9 Hz), 3.69-3.50 (8.3H, m), 3.47-3.38 (0.7H, m), 3.42 (4H, t,

J = 5.9 Hz), 3.10-2.95 (0.7H, m), 2.95- 2.80 (0.3H, m), 1.97 (2H, tt, J = 9 Hz), 1.58-1.30 (2H, m), 1.30-1.02 (4H, m), 0.97 (3H, s), 0.95 (6H, s), 0.74 (3H, t, J = 7.0 Hz).

"C NMR (CD30D): 6/ppm 2,159.8,155.5,155.3,132.4,
8,60.3,53.9,50.3,47.4,46.1,45.7,45.6,40.7,36.3,31.6,30.6,28.0, 7,14.6.

LRMS: (m/z) 529.2 (M+H)+, 527.4 (M-H)-.

MIC (E. coli): 50 pM MIC (S. capitis): 6.25 pLM Example 30 2(R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4- dipropylaminobenzoyl)-2', 2'-dimethylpropyl) amide The title compound was prepared utilising diallyl amine in Step A as described in Scheme 14, and using the General Protocol (GP) thereafter. The final step yielded both Example 30 and Example 31. Relevant spectroscopic data are described below.

STEP A: [1 (S)- (4-Diallylaminobenzoyl)-2, 2-dimethylpropyl]-carbamic acid tert-butyl ester.

Purification by column chromatography (SiO2,19: 1 iso-hexane: ethyl acetate) afforded the title compound as a thick yellow oil (5.18 g, 52% (81% based on recovered SM)).

'H NMR (CDCI3) : 6/ppm 7.89 (2H, d, J = 8.6 Hz), 6.66 (2H, d, J = 8.7 Hz), 5.85 (2H, ddt, J = 7 Hz), 5.47 (1H, brd, J = 9.5 Hz), 5.26-5.11 (4H, m), 5.09 (1 H, d, J = 9.6 Hz), 4.04-3.94 (4H, m), 1.42 (9H, s), 0.95 (9H, s).

#LRMS : (m/z) 387.2 (M+H) +.

STEP GPA: 2 (S)-Amino-1- (4-diallyiamino-phenyl)-3, 3-dimethylbutan-1-one hydrochloride.

The title compound was recovered as yellow solid and used without further purification (3.7 g, 100% crude).

'H NMR (CDOD3): 6/ppm 7.91 (2H, d, J = 8.6 Hz), 6.85 (2H, d, J = 8.7 Hz), 5.90 (2H, ddt, J = 17.1,10.3,4.7 Hz), 5.26-5.17 (3H, m), 5.16-5.12 (1H, m), 4.84 (1H, s), 4.13- 3.05 (4H, m), 1.05 (9H, s).

LRMS: (m/z) 287.2 (M+H} +.

STEP GPB: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(1'(S)-(4-diallylaminobenzoyl)-2', 2'-dimethylpropyl)-amide Purification by column chromatography (SiO2,3: 1 iso-hexane: ethyl acetate) afforded the title compound as a yellow oil (5.64 g, 90%).

'H NMR (CDCl3) : ã/ppm 8.13 (0.6H, brs), 7.95-7.83 (0.4, m), 7.88 (2H, d, J = 9.0 Hz), 7.48-7.31 (5H, m), 6.65 (2H, d, J = 9.1), 6.40 (1 H, d, J = 9.3 Hz), 5.84 (2H, ddt, J = 4,4.7 Hz), 5.44 (1 H, d, J = 9.4 Hz), 5.24-5.17 (3H, m), 5.16-5.10 (1 H, m), 5.08-4.90 (1 H, m), 4.90-4.74 (1 H, m), 4.04-3.94 (4H, m), 3.89-3.58 (2H, m), 2.62-2.48 (1 H, m), 1.60-1.30 (2H, m), 1.30-1.05 (4H, m), 0.91 (9H, s), 0.76 (3H, t, J = 6.9 Hz).

LRMS: (m/z) 548.4 (M+H) +, 570.4 (M+Na) +.

STEP GPC: 2 (R)-[(N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid-(1'(S)-(4-dipropylaminobenzoyl)-2', 2'-dimethylpropyl) amide Purification by reverse phase preparative HPLC yielded the title compound as a colourless foam (20 mg, 22%, 69% combined yield with Example 31).

'H NMR (CD30D): 8/ppm 8.27 (0.3H, s), 7.92-7.80 (2.7H, m), 6.68 (2H, d, J = 9.1 Hz), 5.45 (1H, s), 3.88-3.75 (1H, m), 3.61 (0.3H, dd, J = 14.4,5.8 Hz), 3.48-3.30 (4.7H, m), 3.08-2.90 (0.7H, m), 3.90-2.78 (0.3H, m), 1.64 (4H, qt, J = 7.5,7.5 Hz), 1.55-1.27 (2H, m), 1.27-1.06 (4H, m), 1.05-0.76 (15H, m), 0.74 (3H, t, J = 6.9 Hz).

"C NMR (CD30D): 8/ppm 8,125.8,112.1, 6,27.6,24.0,21.8,14.5,11.9 LRMS: (m/z) 462.2 (M+H) +, 460.4 (M-H)-.

MIC (E. coli): 100 µM MIC (S. capitis): 3.1 iM Example 31 2(R)-[(N-Formyl-N-hydroxyamino)-methyi]-hexanoic acid-(2', 2'-dimethyl-1'(S)-(4- propylaminobenzoyl)-propyl) amide The title compound was prepared in an identical manner to Example 30 as described in Scheme 14. The final step yielded both Example 30 and Example 31.

Relevant spectroscopic data are described below.

STEP GPC: 2 (R)- [ (N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (2', 2'-dimethyl- 1' (S)- (4-propylaminobenzoyl)-propyl) amide Purification by reverse phase preparative HPLC yielded the title compound as a white powder (45 mg, 49%; 69% combined yield with Example 30).

'H NMR (CD30D): B/ppm 8.27 (0.4 H, s), 7.89-7.78 (2.6H, m), 6.60 (2H, d, J=8.9Hz), 5.44 (1 H, s), 3.86-3.72 (1 H, m), 3.61 (0.4H, dd, J=14.0,5.8Hz), 3.40 (0.6H, dd, J=14.2,4.6Hz), 3.13 (2H, t, J=7.1 Hz), 3.08-2.90 (0.6H, m), 3.90-2.76 (0.4H, m), 1.65 (2H, qt, J=7.3,7.3Hz), 1.55-1.30 (2H, m), 1.29-1.06 (4H, m), 1.04-0.89 (12H, m), 0.75 (3H, t, J = 7.0). 13C NMR (CD30D): #/ppm 9,126.7, 3,46.1,45.9,45.7,36.4,31.6,30.6,28.0,24.1,24.0,14.5, 12.3.

LRMS: (m/z) 420.2 (M+H) +, 442.2 (M+Na)+, 418.4 (M-H)-.

MIC (E. coll9: 12.5 1M MIC (S. capitis): 3.1 uM Example 32 2(R)-[(N-formyl-N-hydroxyamino)-methyl]-hexanoicacid-(1'(S)-acetyl-2',2'- dimethylpropyl) amide STEP A: 2 (S)-tert-Butoxycarbonylamino-3,3-dimethyl-butyric acid To a suspension of L-tert-leucine (26.1 g, 0.2 mol) in methanol (150 mL) was added triethylamine (56 mL, 0.4 mol) and the mixture cooled to 0 °C. To the mixture was added slowly a solution of di-tert-butyldicarbamate (48 g, 0.22 mol) in methanol (40 mL) such that an internal temperature of between 0 and 5 °C was maintained. The reaction was allowed to stir overnight and the solvents were removed in vacuo. The residue was dissolved in ethyl acetate (200 mL) and washed with 10% w/v aqueous citric acid solution (3 x 100 mL). The organic layer was dried over MgSO4, filtered and the solvents removed in vacuo to give the title product as a pale yellow oil (48.9 g, >100 %, residual solvent).

'H NMR (CDC): 6/ppm 9.20 (1 H, bs), 5.10 (1 H, m), 4.15 (1 H, m), 1.45 (9H, s), 1.00 (9H, s).

STEP B: [1 (S)-(Methoxy-methyl-carbamoyl)-2, 2-dimethyl propyi]-carbamic acid-tert- butyl ester.

To a solution of 2 (S)-tert-butoxycarbonyiamino-3, 3-dimethyl-butyric acid (30 g, 0.13 mol) in dichloromethane (400 mL) was added portionwise 1,1'-carbonyidiimidazole (63.3 g, 0.39 mol). After addition was complete the reaction was allowed to stir for 15 minutes before N-methoxy-N-methylamine hydrochloride (38 g, 0.39 mol) was added and the reaction allowed to stir overnight. The solvents were removed in vacuo and the residue partitioned between ethyl acetate (250 mL) and 1 M HCI (150 mL). The organic phase was washed with 1 M HCI solution (2 x 100 mL), saturated sodium bicarbonate solution (2 x 100 mL) and brine (100 mL). The organic phase was dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (SiO2,30% ethyl acetate in hexanes) afforded the title product as a pale yellow oil (26.5 g, 74 %).

'H NMR (CDCI3): 6/ppm 5.20 (1 H, bd, J = 9.5 Hz), 4.65 (1H, d, J = 10.4 Hz), 3.77 (3H, s), 3.21 (3H, s), 1.43 (9H, s), 0.97 (9H, s).

LRMS: (m/z) 297 (M+Na) +.

STEP C: (1 (S)-Acetyl-2,2-dimethylpropyl) carbamic acid-tert-butyl ester [1 (S)- (Methoxy-methyl-carbamoyl)-2, 2-dimethylpropyl]-carbamic acid-tert-butyl ester (2.0 g, 7.3 mmol) was dissolved in freshiy distille THF under an argon atmosphere.

The solution was cooled to-78 °C whereupon MeLi (15.6 mL, 1.4 M in diethyl ether, 21.9 mmol, 3 eqv) was added dropwise maintaining an internal temperature <-70 °C. The reaction was stirred at-70 °C for 30 minutes before warming to-30 °C for a further 30 minutes. After this time TLC analysis indicated the complete consumption of starting material. Saturated aqueous ammonium chloride solution (10 mL) was added and the reaction allowed to warm to room temperature. The aqueous phase was extracted with ethyl acetate (3 x 30 mL). The organic phases were washed with water (3 x 50 mL) and brine (50 mL), dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil. Purification by column chromatography (SiO2,20 % ethyl acetate in hexanes) afforded the title compound as a colourless oil (1.355 g, 84%).

'H NMR (CDCI3): â/ppm 5.13 (1H, m), 4.16 (1H, bd, J = 10.0 Hz), 2.25 (3H, s), 1.43 . (9H, s), 0.98 (9H, s).

LRMS: (m/z) 252 (M+Na) +.

STEP D: 3 (S)-Amino-4,4-dimethyl-pentan-2-one To a solution of (1 (S)-acetyl-2,2-dimethylpropyl) carbamic acid-tert-butyl ester (700 mg, 2.55 mmol) in dichloromethane (10 mL) at 0 °C was added trifluoroacetic acid (5 mL). The reaction was left at <5 °C for 16 hours before the solvents were removed in vacuo to give a bright yellow oil. The residue was dissolved in methanol (30 mL) and was treated portionwise with Dowex 1X8-400 basic resin until pH 9. Filtration and removal of the solvents in vacuo gave the title compound as a pale yellow oil (-1.0 g, > 100 %, residual water). The material was used without further purification.

'H NMR (CDCI3): 8/ppm 3.28 (1 H, s), 2.21 (3H, s), 1.50 (2H, bs), 0.98 (9H, s).

STEP E: 2 (R)- (N-Benzyloxyaminomethyl)-hexanoic acid- (1' (S)-acetyl-2', 2'- dimethylpropyl) amide To a suspension of 2 (R)- (N-benzyloxyamino-methyl)-hexanoic acid (879 mg, 3.5 mmol, 1.1 eqv) in DMF (10 mL) at 0 °C was added EDC (730 mg, 1.2 eqv) and 1- hydroxybenzotriazole (43 mg, 10 moi%). The mixture was allowed to stir at 0 °C for 45 minutes before a solution of 3 (S)-amino-4,4-dimethyl-pentan-2-one (409 mg, 1 eqv) in DMF (5 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvents were removed in vacuo and the residue dissolved in ethyl acetate (50 mL) and 10% w/v aqueous citric acid (50 mL).

The aqueous phase was extracted with ethyl acetate (3 x 50 mL) and the combined organic layers washed with saturated sodium hydrogen carbonate (100 mL) and brine (2 x 100 mL). The organic phases were dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil. Purification by column chromatography (SiO2,25% ethyl acetate in hexanes) gave the title compound as a . clear oil (412 mg, 36 %).

'H NMR (CDCI3): â/ppm 7.35 (5H, m), 6.73 (1 H, bd, J = 8.7 Hz), 5.68 (1 H, bs), 4.73 (2H, s), 4.54 (1 H, d, J = 8.7 Hz), 3.06 (2H, m), 2.50 (1 H, m), 2.27 (3H, s), 1.70-1.20 (6H, m), 0.98 (9H, s), 0.87 (3H, t, J = 7.0 Hz).

LRMS: (m/z) 363 (M+H)'.

STEP F: 2 (R)- [N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid- (1' (S)-acetyl-2', 2'-dimethylpropyl) amide To a solution of 2 (R)- (N-benzyloxyamino-methyl)-hexanoic acid- (1' (S)-acetyl-2', 2'- dimethylpropyt) amide (400 mg, 1.1 mmol) in dichloromethane (10 mL) at 0 °C was added formylacetic anhydride (0.25 mL, 2.76 mmol, 2.5 eqv) and the reaction allowed to stir at room temperature. After 2 hours TLC analysis indicated complete consumption of the starting material. The solvents were removed in vacuo and the residue azeotroped with toluene (3 x 30 mL). The product was placed under high vacuum to give the title compound as a clear sticky oil (443 mg, >100 %, residual solvent).

'H NMR (CDCI3) : ã/ppm 8.15 (0.7H, bs), 7.90 (0.3H, bs), 7.38 (5H, bs), 6.06 (1H, bd, J = 8.2 Hz), 5.00-4.75 (2H, m), 4.43 (1 H, bd, J = 8.3 Hz), 3.72 (2H, m), 2.53 (1 H, m), 2.24 (3H, s), 1.65-1.40 (2H, m), 1.35-1.10 (4H, m), 0.94 (9H, s), 0.86 (3H, t, J = 6.7 Hz).

LRMS: (m/z) 389 (M-H)-, 391 (M+H) +.

STEP G: 2 (R)- [N-Formyl-N-hydroxyamino)-methyl]-hexanoic acid- (1' (S)-acetyl-2', 2'-dimethylpropyl) amide To a solution of 2 (R)- [N-benzyloxy-N-formylamino)-methyl]-hexanoic acid-(1' (S)- acetyl-2', 2'-dimethylpropyi) amide (200 mg, 0.55 mmol) in methanol (10 mL) under argon was added a slurry of 10% Pd/C (27 mg) in ethyl acetate (5 mL). Hydrogen gas was bubbled through the reaction for 15 minutes after which time the reaction was allowed to stir under a hydrogen atmosphere of 1 bar for two hours. After this time TLC analysis indicated the complete consumption of starting material. The reaction was flushed with argon and filtered through Ceiite. The solvents were removed in vacuo to afford the title compound as a pale orange solid (148 mg, 96%).

'H NMR (CDCI3): 6/ppm 8.38 (0.3H, s), 7.81 (0.7H, s), 6.40 (0.3H, bd, J = 6.9 Hz), 6.25 (0.7H, bd, J = 8. 2 Hz), 4.52 (1 H, m), 4.00 (0.3H, dd, J = 14.7,7.1 Hz), 3.82 <BR> <BR> <BR> <BR> (0.7H, dd, J = 14.2,10.0 Hz), 3.62 (0.3H, dd, J = 14.5,2.8 Hz), 3.47 (0.7H, dd, J = 8 Hz), 2.79 (0.7H, m), 2.65 (0.3H, m), 2.30 (0.9H, s), 2.27 (2.1 H, s), 1.60 (1 H, m), 1.50-1.20 (5H, m), 1.01 (2.7H, s), 0.96 (6.3H, s), 0.88 (3H, t, J = 6.6 Hz).

'3C NMR (CD30D): 6/ppm 2, 30.7,27.8,24.1,14.6.

LRMS: (m/z) 299 (M-H)-, 301 (M+H) +, 323 (M+Na) l.

To a suspension of 2 (R)- (N-benzyloxyamino-methyl)-hexanoic acid (1.430 mg, 5.17 mmol, 1.1 eqv) in DMF (20 mL) at 0 °C was added EDC (1.190 g, 5.64 mmol 1.2 eqv) and 1-hydroxybenzotriazole (84 mg, 10 mol%). The mixture was allowed to stir at 0 °C for 45 minutes before a solution of 2 (S)-amino-N-methoxy-3,3, N-trimethyl- butyramide (900 mg, 4.7 mmol, 1 eqv) in DMF (5 mL) was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvents were removed in vacuo and the residue dissolved in ethyl acetate (75 mL) and 10% w/v aqueous citric acid (50 mL). The aqueous phase was extracted with ethyl acetate (3 x 75 mL) and the combined organic layers washed with saturated sodium hydrogen -carbonate solution (100 mL) and brine (2 x 100 mL). The organic phases were dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (SiO2,25% ethyl acetate in hexanes) gave the title compound as a clear oil (1.43 g, 68 %).

'H NMR (CDC13): 6/ppm 7.35 (5H, m), 6.73 (1 H, bd, J = 10.0 Hz), 5.70 (1 H, bs), 5.05 (1H, d, J = 10. 0 Hz), 4.74 (2H, s), 3.78 (3H, s), 3.20 (3H, s), 3.07 (2H, m), 2.50 (1H, m), 1.65 (1 H, m), 1.45 (1 H, m), 1.25 (4H, m), 0.98 (9H, s), 0.86 (3H, t, J = 7.0 Hz).

LRMS: (m/z) 408 (M+H) +.

STEP C: 2 (R)-[(N-Benzyloxyamino)-methyl]-hexanoic acid-(1'(S)-benzoyl-2', 2'- dimethylpropyl) amide To a solution of 2 (R)- [ (N-benzyloxyamino)-methyl]-hexanoic acid- [1' (S)- (methoxy- methyl-carbamoyi)-2', 2'-dimethylpropyl] amide (416 mg, 1.05 mmol) in freshly distilled THF (10 mL) under argon at-78 °C was added dropwise PhLi (3.5 mL, 1.8M in cyclohexane, 6.3 mmol, 6 eqv) such that an internal temperature of <-70 °C was maintained. The reaction was allowed to stir at-70 °C for three hours after which time TLC analysis appeared to indicate the complete consumption of starting material. Saturated aqueous ammonium chloride solution (10 mL) was added and the solution allowed to warm to room temperature. The aqueous phase was extracted with ethyl acetate (3 x 50 mL), and the organic phases combined and washed with water (3 x 50 mL) and brine (50 mL). The organic phase was dried over MgSO4, filtered and the solvents removed in vacuo to give a crude yellow oil.

Purification by column chromatography (si02/25 % ethyl acetate in hexanes) gave the title product as a colourless oil (143 mg, 32 %, Rf = 0.3) and the recovered starting material 2 (R)- [ (N-Benzyloxyamino)-methyl]-hexanoic acid- [1' (S)- (methoxy- methyl-carbamoyl)-2', 2'-dimethylpropyl] amide (209 mg, Rf = 0.1).

'H NMR (CDCI3): 8/ppm 8.02 (2H, m), 7.62-7.40 (2H, m), 7.40-7.25 (6H, m), 6.97 #(1H, bd, J = 9. 4 Hz), 5.60 (1H, d, J = 9.4 Hz), 4.75 (2H, s), 3.10 (2H, m), 2.53 (1H, m), 1.65-1.30 (2H, m), 1.30-1.10 (4H, m), 0.94 (9H, s), 0.85 (3H, m).

STEP D: 2 (R)-[(N-Benzyloxy-N-formylamino)-methyl]-hexanoic acid-(1'(S)-benzoyl- 2', 2'-dimethylpropyl) amide To a solution of 2 (R)-[(N-benzytoxyamino)-methyl]-hexanoic acid-(1'(S)-benzoyl-2', 2'-dimethylpropyl) amide (195 mg, 0.46 mmol) in dichloromethane (50 mL) at 0 °C was added formylacetic anhydride (0.1 mL, 1.15 mmol, 2.5 eqv) and the reaction allowed to stir at room temperature. After 1 hour TLC analysis indicated complete consumption of the starting material. The solvents were removed in vacuo and the residue azeotroped with toluene (3 x 30 mL). The product was placed under high vacuum for several hours to give the title compound as a clear sticky oil (208 mg, 100%).

'H NMR (CDCI3): 6/ppm 8.15 (0.5H, bs), 8.00 (2.5H, m), 7.65-7.30 (8H, m), 6.33 (1H, bd, J = 9.0 Hz), 5.51 (1 H, d, J = 9.0 Hz), 5.00 (1 H, m), 4.80 (1 H, m), 3.75 (2H, bm), 2.58 (1 H, m), 1.70-1.00 (6H, m), 0.89 (9H, s), 0.77 (3H, t, J = 6.7 Hz).

LRMS: (m/z) 451 (M-H)-, 453 (M+H) +.

STEP E: 2 (R)-[(N-Formyl-N-hyd roxyamino)-methyl]-hexanoic acid-(1'(S)-benzoyl- 2', 2'-dimethylpropyl) amide To a solution of 2 (R)- [ (N-benzyloxy-N-formylamino)-methyl]-hexanoic acid-(l' (S)- benzoyl-2', 2'-dimethylpropyl) amide (192 mg, 0.43 mmol) in methanol (5 mL) was added a slurry of 10% Pd/C (20 mg) in ethyl acetate (2 mL). Hydrogen gas was bubbled through the reaction for 15 minutes after which time the reaction was allowed to stir under a hydrogen atmosphere of 1 bar for. After four hours reaction time TLC analysis indicated the complete consumption of starting material.

The reaction was flushed with argon and filtered through glass fibre. The solvents were . removed in vacuo to afford the title compound as a white crystalline solid (135 mg, 88%). The product was purified by preparative HPLC giving 75 mg (49 %) of a white crystalline solid.

'H NMR (CDCI3): 6/ppm 9.18 (1H, bs), 8.40 (0.3H, s), 8.00 (2H, bd, J = 7.1 Hz), 7.86 (0.7H, s), 7.60 (1 H, m), 7.48 (2H, m), 6.84 (0.3H, bd, J = 9.2 Hz), 6.70 (0.7H, bd, J = 9.3 Hz), 5.55 (1H, m), 4.05 (0.3H, dd, J = 14.6,7.2 Hz), 3.87 (0.7H, dd, J = 14.1,9.7 Hz), 3.64 (0.3H, dd, J = 14.6,3.3 Hz), 3.47 (0.7H, dd, J = 14.0,4.0 Hz), 2.85 (0.7H, m), 2.71 (0.3H, m), 1.55 (1H, m), 1.40 (1 H, m), 1.30-1.10 (4H, m), 0.94 (3H, s), 0.90 (6H, s), 0.78 (3H, t, J = 6.3 Hz).

'3C NMR (CDCI3): 6/ppm 6,133.9,133.6,128.9,128.8,128.6, 8,29.2,29.1,27.0,22.5,13.7.

LRMS: (m/z) 361 (M-H)-, 363 (M+H) +.

Biological Example Minimal inhibitory concentrations (MIC) of inhibitors against E. coli strain DH5a <BR> <BR> <BR> deoRrecA1endA1hsdR17(rk,(Genotype;F-#80d/acZ#M15#(lacZYA-argF)U169 mk') phoA supE44 ~ thi-1 gyrA96 re/A1) obtained from GibcoBRL Life Technologies, or Staphylococcus capitis (American Type Culture Collection number 35661) were determined as follows. Stock solutions of each test compound were prepared by dissolution of the compound in dimethylsulfoxide at 1 OmM. For the determination of . the minimal inhibitory concentration, two fold serial dilutions were prepared in 2xYT broth (typtone 16g/1, yeast extract 1 Og/1, sodium chloride 5g/1 obtained from BIO 101 Inc, 1070 Joshua Way, Vista, CA92083, USA) to yield 0.05 mi compound-containing medium per well. Inocula were prepared from cultures grown overnight in 2xYT broth at 37° C. Cell densities were adjusted to absorbance at 660nm (A660) = 0.1; the optical density-standardised preparations were diluted 1: 1000 in 2xYT broth; and each well inoculated with 0.05ml of the diluted bacteria. Microtiter plates were incubated at 37°C for 18 hours in a humidified incubator. The MIC ( M) was recorded as the lowest drug concentration that inhibited visible growth.

Claims 1. The use of a compound of formula (I) or a pharmaceutically or veterinarily acceptable salt, hydrate or solvate thereof in the preparation of a composition for treatment of bacterial or protozoal infections in humans and non-human mammals: wherein: Z represents a radical of formula-N (OH) CH (=O) of formula-C (=O) NH (OH); R, represents hydrogen, methyl or trifluoromethyl, or, except when Z is a radical of formula-N (OH) CH (=O), a hydroxy or amino group; R2 represents a group Rro-(X) n-(ALK) m-wherein R10 represents hydrogen, or a C,-Cs alkyl, C2-C6 alkenyl, C2-C6 alkynyl, cycloalkyl, aryl, or heterocyclyl group, any of which may be unsubstituted or substituted by (Ci-Ce) alkyl, (C,-C6) alkoxy, hydroxy, mercapto, (C,-C6) alkylthio, amino, halo (including fluoro, chloro, bromo and iodo), trifluoromethyl, cyano, nitro, oxo,-COOH,-CONH2-COORA,-NHCORA,-CONHRA,-NHRA,-NRARB, or-CONRARB wherein RA and RB are independently a (Ci-Ce) alkyl group and ALK represents a straight or branched divalent C,-Cs alkylene, C2-C6 alkenylene, or C2-C6 alkynylene radical, and may be interrupted by one or more non-adjacent-NH-,-O-or-S-linkages, X represents-NH-,-O-or-S-, and m and n are independently 0 or 1; R3 represents the side chain of a natural or non-natural alpha amino acid; and R4 represents a radical R5- (ALK) P- wherein ALK is as defined in relation to R2, p is 0 or 1, and R, represents hydrogen, or a C,-C6 alkyl, C2-C6 alkenyi, C2-Cs alkynyl, cycloalkyl, aryl, or heterocyclyl group any of which (i) may be substituted by a group selected from (C,-C6) alkyl, phenyl, benzyl, (C1-C6) alkoxy, phenoxy, hydroxy, mercapto, (C1-C6) alkylthio, amino, halo, trifluoromethyl, cyano, nitro, oxo,-COOH,-SO2H,-CONH2.-SO2NH2,-CORA, -SO2RA,-COORA,-CONHRA,-SO2NHRA,-NHCORA,-SORA,-SO2RA, -NHSO2RA, and-NHRA, wherein RA is (C,-C6) alkyl, cycloalkyl, phenyl, 2-, 3-or 4-pyridyl, N-or 2-, 3-or 4- piperidyl, N-or 2-or 3-piperazyl group; or (ii) may be substituted by-NRARB, -CONRARB or-SO2NRARB, wherein RA and RB are independently (C,-C6) alkyl, cycloalkyl, phenyl, 2-, 3-or 4-pyridyl, N-or 2-, 3-or 4- piperidyl, N-or 2-or 3-piperazyl group, or when taken together with the N atom to which they are attached RA and RB form

a 5 to 7 membered aromatic or non-aromatic ring, which ring (a) may contain addition heteroatoms selected from N, O and S, and in which any S atom may be oxidised as a sulphonyl or sulphoxide, and (b) may be substituted on a ring carbon or heteroatom by one or more of the substituents listed under (i) above.

2. A method for the treatment of bacterial or protozoal infections in humans and non-human mammals, which comprises administering to a subject suffering such infection an antibacterially or antiprotozoally effective dose of a compound of formula (I) as defined in claim 1.

3. A compound of formula (I) as set forth in claim 1 wherein Z is a radical of formula-N (OH) CH (=O), or a a pharmaceutically or veterinarily acceptable salt, hydrate or solvate thereof.

4. A compound of formula (I) as set forth in claim 1 wherein Z is a radical of formula-C (=O) NH (OH) and R4 represents a radical R5- (ALK) P- wherein ALK is as defined in relation to R2, p is 0 or 1, and R5 represents hydrogen, or a C,-C6 alkyl, C2- C6 alkenyl, C2-C6 alkynyl, cycloalkyl, aryl, or heterocyclyl group which is substituted by-NRARe,-CONR"RB or-SO2NRARB, wherein RA and R8 taken together with the N . atom to which they are attached form a 5 to 7 membered aromatic or non-aromatic ring, which ring (a) may contain additional heteroatoms selected from N, O and S, and in which any S atom may be oxidised as a sulphonyl or sulphoxide, and (b) may be substituted by a group selected from (C,-C6) alkyl, phenyl, benzyl, (C,-C6) alkoxy, phenoxy, hydroxy, mercapto, (Cl-C6) alkylthio, amino, halo, trifluoromethyl, cyano, nitro,-SO2H,-CONH2,-SO2NH2,-CORA,-SORA,-SO2RA,-SO2RA,--COOH, -SO2NHRA,-NHCORA,-NHSO2RA,and-NHRA,whereinRAisCOORA,-CONHRA, Ci-C6) alkyl, cycloalkyl, phenyl, 2-, 3-or 4-pyridyl, N-or 2-, 3-or 4-piperidyl, N-or 2- or 3-piperazyl group, or a a pharmaceutically or veterinarily acceptable salt, hydrate or solvate thereof.

5. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R, is hydrogen.

6. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R2 is: optionally substituted C,-Cg alkyl, C3-C6 alkenyl, C3-C6 alkynyl or cycloalkyl; phenyl (C,-C6 alkyl)-, phenyl (C3-CB alkenyl)-or phenyl (C3-C6 alkynyl)- optionally substituted in the phenyl ring; cycloalkyl (C,-C6 alkyl)-, cycloalkyl (C3-C6 alkenyl)-or cycloalkyl (C3-C6 alkynyl)-optionally substituted in the cycloalkyl ring; heterocyclyl (C,-C6 alkyl)-, heterocyclyl (C3-C6 alkenyl)- or heterocyciyl (C3-C6 alkynyl)-optionally substituted in the heterocyclyl ring; or CH3 (CH2) pO (CH2) q- or CH3 (CH2) pS (CH2) q-, wherein p is 0,1,2 or 3 and q is 1, 2 or 3.

7. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R2 is methyl, ethyl, n-or iso-propyl, n-and iso- butyi, n-pentyl, iso-pentyl, 3-methyl-but-1-yl, n-hexyl, n-heptyl, n-acetyl, n-octyl, methylsulfanylethyl, ethylsulfanylmethyl, 2-methoxyethyl, 2-ethoxyethyl, 2- ethoxymethyl, 3-hydroxypropyl, allyl, 3-phenylprop-3-en-1-yl, prop-2-yn-1-yl, 3-phenylprop-2-yn-1-yl, 3- (2-chlorophenyl) prop-2-yn-1-yl, but-2-yn-1-yl, cyclopentyl, cyclohexyl, cyclopentylmethyl, cyclopentyl ethyl, cyclopentylpropyl, cyclohexylmethyl, cyclohexylethyl, cyclohexylpropyl, furan-2-ylmethyl, furan-3-methyl, tetrahydrofuran- 2-ylmethyl, tetrahydrofuran-2-ylmethyl, piperidinylmethyl, phenylpropyl, 4- chlorophenylpropyl, 4-methylphenylpropyl, 4-methoxyphenylpropyl, benzyl, 4- chlorobenzyl, 4-methylbenzyl, or 4-methoxybenzyl.

8. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R2 is n-propyl, n-butyl, n-pentyl, or cyclopentylmethyl.

9. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or

claim 4 wherein R3 is: the characterising group of a natural a amino acid, for example benzyl, or 4-methoxyphenylmethyl, in which any functional group may be protected, any amino group may be acylated and any carboxyl group present may be amidated; or a group-[Alk]0R9 where Alk is a (C,-C6) alkylene or (C2-C6) alkenylene group optionally interrupted by one or more-O-, or-S-atoms or-N (R, 2)-groups [where R12 is a hydrogen atom or a (Ci-Ce) alkyl group], n is 0 or 1, and Rg is hydrogen or an optionally substituted phenyl, aryl, heterocyclyl, cycloalkyl or cycloalkenyl group or (only when n is 1) Rg may addition be hydroxy, mercapto, (C1-C6) alkylthio, amino, halo, trifluoromethyl, nitro,-COOH,--CONHRA,-NHRA,-NRARB,or-CORNRARBCONH2,-COORA,-NHCORA, wherein RA and R'are independently a (C,-C6) alkyl group; or a benzyl group substituted in the phenyl ring by a group of formula - R8ishydroxyl,amino,(C1-C6)alkoxy,phenyl(C1-C6)alkoxy,OCH2COR8where (C1-C6) alkylamino, di ((C,-C6) alkyl) amino, phenyl (C,-C6) alkylamino; or a heterocyclic (C,-C6) alkyl group, either being unsubstituted or mono-or di- substituted in the heterocyclic ring with halo, nitro, carboxy, (C1-C6) alkoxy, cyano, (Ci-Ce) alkanoyl, trifluoromethyl (C1-C6)alkyl, hydroxy, formyl, amino, (Ci-C6) alkylamino, di-(C1-C6)alkylamino, mercapto, (Ci-Ce) alkylthio, or(C1-C6) alkylphenylmethyl;orhydroxy(C1-C6)alkyl,mercapto(C1-C6)alkyl a group -CRaRbRc in which: each of Ra, Rb and Rc is independently hydrogen, (C,-C6) alkyl, (C2- phenyl(C1-C6)alkyl,(C3-C8) cycloalkyl;orC6)alkenyl,(C2-C6)alkynuyl, Rc is hydrogen and Ra and Rb are independently phenyl or heteroaryl such as pyridyl; or Rc is hydrogen, (C1-C6) alkyl, (C2-C6) alkenyl, (C2-C6) alkynyl, phenyl (C,- C6) alkyl, or (C3-C8) cycloalkyl, and Ra and Rb together with the carbon atom to which they are attached form a 3 to 8 membered cycloalkyl or a 5-to 6-membered heterocyciic ring; or Rai Rb and Rz together with the carbon atom to which they are attached form a tricyclic ring (for example adamantyl); or Ra and Rb are each independently (C,-C6) alkyl, (C2-C6) alkenyl, (C2- C6) alkynyl, phenyl (C,-C6) alkyl, or a group as defined for Rc below other than hydrogen, or Ra and Rb together with the carbon atom to which they are attached form a cycloalkyl or heterocyclic ring, and Rc is -SH,hydrogen,-OH, -CO2H,(C1-C4)perfluoroalkyl,--CN, -O(C1-C6)alkyl,-O(C2-C6)alkenyl,-S(C1-CH2OH,-CO2(C1-C6) alkyl, C6) alkyl,-SO (C,-C6) alkyl,-SO2 (C,-C6) alkyl,-S (C2-C6) alkenyl,-SO (C2- Ce) alkenyi,-SO2 (C2-C6) alkenyl or a group-Q-W wherein Q represents a bond or-O-,-S-,-SO-or-SO2-and and W represents a phenyl, phenylalkyl, (C3-C8) cycloaikyl, (C3-C8) cycloalkylalkyl, (C4-heteroarylorheteroarylalkylC8(cycloalkenyl,(C4-C8)cycloalkenylalkyl, group, which group W may optionally be substituted by one or more substituents independently selected from, hydroxyl, halogen,-CN,- -CONH2,-CONH(C1-C6)alkyl,-CONH(C1-CO2H,-CO2(C1-C6)alkyl, -CH2OH,(C1-C4) perfluoroalkyl,-O(C1-C6)alkyl,-S(C1-C6alkyl)2,-CH0, C6) alkyl,-SO (C,-Cs) alkyl,-SO2 (C,-C6) alkyl,-N02,-NH2,-NH (C,-C6) alkyl, (C1-C6)alkyl,(C2-C6)alkenyl,(C2--N((C1-C6)alkyl)2,-NHCO(C1-C6) alkyl, C6) alkynyl, (C3-C8) cycloalkyl, (C4-C8) cycloalkenyl, phenyl or benzyl.

10. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R3 is methyl, ethyl, benzyl, 4-chlorobenzyl, 4- hydroxybenzyl, phenyl, cyclohexyl, cyclohexylmethyl, pyridin-3-ylmethyl, tert- butoxymethyl, naphthylmethyl, iso-butyl, sec-butyl, tert-butyl, 1-benzylthio-1- methylethyl, 1-methylthio-1-methylethyl, 1-mercapto-1-methylethyl, 1-methoxy-1-<BR> methylethyl, 1-hydroxy-1-methylethyl, 1-fluoro-1-methylethyl, hydroxymethyl, 2- hydroxethyl, 2-carboxyethyl, 2-methylcarbamoylethyl, 2-carbamoylethyl, or 4- aminobutyl.

11. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R3 is tert-butyl.

12. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R4 is: optionally substituted C,-C8 alkyl, C2-C6 alkenyl, C2-C6 alkynyl or cycloalkyl; optionally substituted phenyl, biphenyl or naphthyl; optionally substituted piperidinyl, cyclohexyl, cyclopentyl, oxazolyl, thiazepinyl, pyridinyl, pyrrolidinyl, pyrimidinyl, morpholinyl, piperazinyl, indolyl, thienyl, furanyl, pyrrolyl, imidazolyl, benzofuranyl, benzothienyl, benzimidazolyl, thiazolyl, benzothiazolyl, pyrazolyl, isoxazolyl, isothiazolyl,<BR> triazolyl, thiadiazolyl, oxadiazolyl, pyridinyl,

pyridazinyl, pyrazinyl, or triazinyl. phenyl(C2-C6alkenyl)-orphenyl(C2-C6alkynyl)-phenyl(C1-C6alkyl)-, optionally substituted in the phenyl ring; cycloalkyl (C,-C6 alkyl)-, cycloalkyl (C2-C6 alkenyl)-or cycloalkyl (C2-C6 alkynyl)- optionally substituted in the cycloalkyl ring; heterocyclyl (C,-C6 alkyl)-, heterocyclyl (C2-C6 alkenyl)-or heterocyclyl (C2-C6 alkynyl)-optionally substituted in the heterocyclyl ring.

13. A use as claimed in claim 1, a method as claimed in claim 2, or compound as claimed in claim 3 or claim 4 wherein R4 is: methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 2-phenylcycloprop-1-yl, benzyl, biphenyl-2-yl, biphenyl-3-yl, biphenyl-4-yl, 2-methoxyphenyl, 3-methoxyphenyl, 4- methoxyp[henyl, 3,4-dimethoxyphenyl,2,4-dimethoxyphenyl, 2-phenoxyphenyl, 3-phenoxyphenyl, 4-phenoxyphenyl, 2-fluorophenyl, 3- fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4- dichlorophenyl, 3-bromophenyl,4-bromophenyl,2-bromophenyl, 2-iodophenyl, 3-iodophenyl, 4-iodophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 3,4-dimethyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2- acetamidophenyl, 3-acetamidophenyl, 4-acetamidophenyl, 2-N, N- dimethylaminophenyl, 3-N, N-dimethylaminophenyl, 4-N, N-dimethylaminophenyl, 2- methanesulfonamidophenyl, 3-methanesulfonamidophenyl, 4- 3-hydroxyphenyl,4-hydroxyphenyl,methanesulfonamidophenyl,2-hydroxyphenyl, .2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 2-thiophenolyl, 3- thiophenolyl, 4-thiophenolyl, 2-thioanisolyl, 3-thioanisolyl, 4-thioanisolyl, 1-naphthyl, thien-2-yl,pyrrol-2-yl,1-methylpyrrol-2-yl,imidazol-2-yl,1-2-naphthyl,furan-2-yl, methylimidazol-2-yl, thiazol-2-yl, 5-phenylpyrrol-2-yl, 5-phenylfuran-2-yl, 5- jphenylthien-2-yl, benzothiazol-2-yl, 1,2,4-oxadiazol-5-yl, 3-methyl-1,2,4-oxadiazol-5- yl, 3-phenyl-1,2,4-oxadiazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,3,4-oxadiazol-2-yl, 1,2,4-thiadiazol-5-yl, 1,3,4-thiadiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxides of pyridin-2-yl pyridin-3-yi and pyridin-4-yl, indol-2-yl, indol-3-yl, 1-methylindol-2-yl, 1- methylindol-3-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, pyrazin-2-yl, 1,2- pyridazin-3-yi, 1,3-pyrimidin-2-yl, benzo [b] thien-2-yl, benzo [b] thien-3-yl, benzo [b] furan-2-yl, benzo [b] furan-3-yl, isoxazol-5-yl, quinolin-2-yl, quinolin-3-yi, 2-oxo-2-phenylethyl,diphenylmethyl,4-N-isoquinolin-2-yl,isoquinolin-3-yl, methylaminophenyl, 4-N, N-dimethylcarboxamidophenyl, and 4-carboxyphenyl.

14. A use as claimed in claim 1, a method as claimed in claim 2, a compound as claimed in claim 3 or claim 4 wherein R4 is a phenyl group which is substituted by one of the following: 15. A compound which is specifically named and characterised in any of Examples 1 to 32 herein.

16. A pharmaceutical composition comprising a compound as claimed in claim 3 or claim 4, or any of claims 5 to 15 together with a pharmaceutically acceptable carrier.

Description ClaimsDescription Claims